they are endemic mostly in arid and tropical areas. Different **venoms** and clinical presentations are seen across the different species. Most commonly, an inflammatory local reaction occurs with **envenomation**, which is **treated** with wound debridement and cleaning, tetanus prophylaxis, and antihistamines. Occasionally the **venom** is allergenic, and the resultant allergic reaction is **treated** in a standard fashion.(ABSTRACT TRUNCATED AT 400 WORDS)

L37 ANSWER 4 OF 5 MEDLINE
ACCESSION NUMBER: 88116573 MEDLINE
DOCUMENT NUMBER: 88116573 PubMed ID: 2892880
TITLE: Erythema nodosum following a **jellyfish** sting.
AUTHOR: Auerbach P S; Hays J T
CORPORATE SOURCE: Vanderbilt University Hospital, Nashville, Tennessee.
SOURCE: JOURNAL OF EMERGENCY MEDICINE, (1987 Nov-Dec) 5 (6) 487-91.
Journal code: IBO; 8412174. ISSN: 0736-4679.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198803
ENTRY DATE: Entered STN: 19900308
Last Updated on STN: 19950206
Entered Medline: 19880318

AB At least 100 of the approximately 9,000 species of coelenterates are dangerous to humans. The most common syndrome following an **envenomation** is an immediate intense dermatitis, with characteristic skin discoloration, local pain, and systemic symptoms. In this case report, we describe a case of erythema nodosum with articular manifestations following **envenomation** with an unknown **jellyfish**. Serological testing of the victim revealed marked elevation of immunoglobulins G and M directed against Physalia physalis, the Portuguese man-of-war. The patient's condition did not respond to conventional topical **therapy** for coelenterate **envenomation**, but was successfully managed with systemic **corticosteroid therapy**. This case demonstrates that the emergency physician should consider a delayed reaction to a marine **envenomation** in any victim who presents with an acute dermatological disease following immersion in marine coastal waters.

*Bites and Stings: CO, complications
*Cnidaria
Cnidaria: IM, immunology
*Emergencies
*Erythema Nodosum: ET, etiology
IgG: AN, analysis
IgM: AN, analysis
***Jellyfish**
Jellyfish: IM, immunology
Middle Age
Synovitis: ET, etiology

L37 ANSWER 5 OF 5 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1993:395580 BIOSIS
DOCUMENT NUMBER: PREV199396070880
TITLE: Envenomation caused by poisonous animals.
AUTHOR(S): Azevedo-Marques, Marisa M. De (1); Cupo, Palmira; Hering, Sylvia Evelyn
CORPORATE SOURCE: (1) Dep. Clinica Medica Faculdade Med. Ribeirao Preto-USP
SOURCE: Medicina (Ribeirao Preto), (1992) Vol. 25, No. 4, pp. 539-554.
ISSN: 0076-6046.
DOCUMENT TYPE: Article
LANGUAGE: Portuguese
SUMMARY LANGUAGE: Portuguese; English

AB Pathophysiological, clinical and **therapeutical** aspects of **envenomation** caused by most common poisonous animals in Southwest of Brazil are described. **Envenomation** caused by snakes of genera Bothrops, crotalus or Micrurus, by **spiders** of genera Loxosceles and Phoneutria and by scorpions of genera Tityus are discussed. When indicated, **antivenom** serotherapy must be given by intravenous route, without dilution, drop by drop and preceded by anti-histamine (H-1 - and H-2 - antagonists) as well **corticosteroids** in order to prevent or reduce hypersensitivity reactions, without needing of skin

tests.

ACCESSION NUMBER: 1998:394209 CAPLUS
DOCUMENT NUMBER: 129:58813
TITLE: Gel formulations for topical drug delivery
INVENTOR(S): Beaurline, Joseph M.; Roddy, Patrick J.; Tomai, Mark A.
PATENT ASSIGNEE(S): Minnesota Mining and Manufacturing Company, USA
SOURCE: PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9824436	A2	19980611	WO 1997-US21995	19971201
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9853686	A1	19980629	AU 1998-53686	19971201
AU 723897	B2	20000907		
EP 942724	A2	19990922	EP 1997-950772	19971201
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE, PT, IE				
BR 9713677	A	20000328	BR 1997-13677	19971201
JP 2001501968	T2	20010213	JP 1998-525740	19971201
NO 9902638	A	19990716	NO 1999-2638	19990601

PRIORITY APPLN. INFO.: US 1996-759992 A 19961203
WO 1997-US21995 W 19971201

AB Pharmaceutical gel formulations for topical drug delivery include drug, colloidal silicon dioxide, triacetin, and propylene glycol. The gel formulations are well suited for topical delivery of the drug 4-amino-2-ethoxymethyl-.alpha.,.alpha.-dimethyl-1H-imidazo[4,5-c]quinoline-1-ethanol, which when applied topically induces cytokines, such as interferon and tumor necrosis factor, locally in the skin or mucous membranes of a mammal. The gel formulations are also well suited for topical delivery of drugs for treatment of diseases involving skin and/or mucosal lesions because the gel formulations do not need to include irritating components.

IT **144875-48-9**
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(topical gels contg. imidazoquinolinethanol deriv. for enhancement of immune responses)

ACCESSION NUMBER: 89313407 MEDLINE
DOCUMENT NUMBER: 89313407 PubMed ID: 2664428
TITLE: Acute arthropod envenomation. Incidence, clinical features and management.
AUTHOR: Binder L S
CORPORATE SOURCE: Division of Emergency Medicine, Texas Tech University Regional Academic Health Center, El Paso.
SOURCE: MEDICAL TOXICOLOGY AND ADVERSE DRUG EXPERIENCE, (1989 May-Jun) 4 (3) 163-73. Ref: 84
Journal code: MTD; 8709214. ISSN: 0112-5966.
PUB. COUNTRY: New Zealand
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198908
ENTRY DATE: Entered STN: 19900309
Last Updated on STN: 19900309
Entered Medline: 19890825
AB Black widow spider (Latrodectus mactans) **envenomation** is found throughout both the temperate and tropical latitudes, and is one of the leading causes of death from arthropod **envenomations** worldwide. The **venom** is highly neurotoxic, affecting the presynaptic motor endplate to allow massive noradrenaline (norepinephrine) and acetylcholine release into synapses causing excessive stimulation and fatigue of the motor end plate and muscle. Clinically, patients develop a bite site lesion and pain, abdominal pain and tenderness, and lower extremity pain and weakness within minutes to hours of **envenomation**. Symptoms progress over several hours, then subside over 2 to 3 days. The recommended **treatment** of 'common' **envenomation** is calcium gluconate 10% intravenously, titrated to relief of symptoms; antivenin, although effective, may cause hypersensitivity and serum sickness reactions, and should be restricted to life-threatening **envenomations** only. Brown recluse spider (Loxosceles reclusa) **envenomations** are seen in the Americas and in Europe, and are endemic to the south and central United States. The **venom** contains at least 8 enzymes, consisting of various lysins (facilitating **venom** spread) and sphingomyelinase D, which causes cell membrane injury and lysis, thrombosis, local ischaemia, and chemotaxis. Local **envenomations** begin as pain and itching that progresses to vesiculation with violaceous necrosis and surrounding erythema, and ultimately ulcer formation. Systemic **envenomations** may be life threatening, and present with fever, constitutional symptoms, petechial eruptions, thrombocytopenia, and haemolysis with haemoglobinuric renal failure. **Treatment** of local **envenomations** is conservative (local wound care, cryotherapy, elevation, tetanus prophylaxis, and close follow-up); systemic **envenomation** requires supportive care and **treatment** of arising complications, **corticosteroids** to stabilise red blood cell membranes, and support of renal function. Dapsone 100mg daily has emerged as a promising **therapeutic** agent in both animal studies and clinical trials. Over 650 species of scorpions are known to cause **envenomation** (mostly in children under 10 years); they are endemic mostly in arid and tropical areas. Different **venoms** and clinical presentations are seen across the different species. Most commonly, an inflammatory local reaction occurs with **envenomation**, which is **treated** with wound debridement and cleaning, tetanus prophylaxis, and antihistamines. Occasionally the **venom** is allergenic, and the resultant allergic reaction is **treated** in a standard fashion.(ABSTRACT TRUNCATED AT 400 WORDS)

ACCESSION NUMBER: 2001496612 IN-PROCESS
DOCUMENT NUMBER: 21427974 PubMed ID: 11545249
TITLE: Role of crotoxin, a phospholipase A2 isolated from Crotalus durissus terrificus snake venom, on inflammatory and immune reactions.
AUTHOR: Cardoso D F; Lopes-Ferreira M; Faquim-Mauro E L; Macedo M S; Farsky S H
CORPORATE SOURCE: Laboratory of Immunopathology, Institute Butantan, Sao Paulo, Brazil.
SOURCE: MEDIATORS OF INFLAMMATION, (2001 Jun) 10 (3) 125-33. Journal code: C2M; 9209001. ISSN: 0962-9351.
PUB. COUNTRY: England: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE: Entered STN: 20010910
Last Updated on STN: 20010910

AB BACKGROUND: Crotoxin (CTX) is a potent neurotoxin from Crotalus durissus terrificus snake **venom** (CdtV) composed of two subunits: one without catalytic activity (crotapotin), and a basic phospolipase A2. Recent data have demonstrated that CdtV or CTX inhibit some immune and inflammatory reactions. AIM: The aim of this paper was to investigate the mechanisms involved in these impaired responses. MATERIALS AND METHODS: Male Swiss mice were bled before and at different intervals of time after subcutaneous injection of CTX or bovine serum albumin (BSA) (control animals). The effect of **treatments** on circulating leukocyte mobilisation and on serum levels of interleukin (IL)-6, IL-10, interferon (IFN)-gamma and **corticosterone** were investigated. Spleen cells from **treated** animals were also stimulated in vitro with concanavalin A to evaluate the profile of IL-4, IL-6, IL-10 or IFN-gamma secretion. Cytokine levels were determined by immunoenzymatic assay and **corticosterone** levels by radioimmunoassay. To investigate the participation of endogenous **corticosteroid** on the effects evoked by CTX, animals were **treated** with metyrapone, an inhibitor of glucocorticoid synthesis, previous to CTX **treatment**. RESULTS: Marked alterations on peripheral leukocyte distribution, characterised by a drop in the number of lymphocytes and monocytes and an increase in the number of neutrophils, were observed after CTX injection. No such alteration was observed in BSA-**treated** animals. Increased levels of IL-6, IL-10 and **corticosterone** were also detected in CTX-injected animals. IFN-gamma levels were not modified after **treatments**. In contrast, spleen cells obtained from CTX-**treated** animals and stimulated with concanavalin A secreted less IL-10 and IL-4 in comparison with cells obtained from control animals. Metyrapone pretreatment was effective only to reverse the neutrophilia observed after CTX administration. CONCLUSIONS: Our results suggest that CTX may contribute to the deficient inflammatory and immune responses induced by crude CdtV. CTX induces endogenous mechanisms that are responsible, at least in part, for these impaired responses.

L37 ANSWER 1 OF 5 MEDLINE
ACCESSION NUMBER: 96431938 MEDLINE
DOCUMENT NUMBER: 96431938 PubMed ID: 8835004
TITLE: [Case report of **jellyfish** injury].
Fallstudie einer Quallenverletzung.
AUTHOR: Raupp U; Milde P; Goerz G; Plewig G; Burnett J; Heeger T
CORPORATE SOURCE: Hautklinik, Heinrich-Heine-Universitat, Dusseldorf.
SOURCE: HAUTARZT, (1996 Jan) 47 (1) 47-52.
Journal code: G13; 0372755. ISSN: 0017-8470.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: German
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199612
ENTRY DATE: Entered STN: 19970128
Last Updated on STN: 19970128
Entered Medline: 19961204

AB We are presenting a 47-year-old woman who was stung by **jellyfish** while bathing in the sea of Thailand. Immediately after the injury she developed sharp pain and urticarial erythema of the skin of the knees accompanied by muscle cramps of the entire body. After a few days a toxic contact dermatitis with edematous swelling and ulcerations developed, which did not respond to topical antibiotics or **corticosteroids**. Three weeks later the patient presented with a disseminated urticarial eruption, which at first responded well to topical **treatment** and systemic **corticosteroids**. Over the next few weeks, however, a relapse of the eruption and the ulcerations occurred. Raised titres of IgG and IgM antibodies against different **jellyfish** from the Indian and Pacific Ocean were detected in the patient's serum by the enzyme-linked immunosorbent assay. Antibodies against bees (class 1) and wasps (class 4) were found by the radioallergosorbent test. The clinical features and the immunological findings led to the diagnosis of toxic and allergic contact dermatitis to **jellyfish venom**. First aid and secondary **treatment** of **jellyfish** injuries are suggested.

CT . . .
Dermatitis, Allergic Contact: DT, drug therapy
Dermatitis, Allergic Contact: IM, immunology
Enzyme-Linked Immunosorbent Assay
IgG: BL, blood
IgM: BL, blood
***Jellyfish**
Jellyfish: IM, immunology
Middle Age
Radioallergosorbent Test
Skin: IM, immunology
*Skin: IN, injuries

L37 ANSWER 2 OF 5 MEDLINE
ACCESSION NUMBER: 91033392 MEDLINE
DOCUMENT NUMBER: 91033392 PubMed ID: 2227687
TITLE: Brown **spider** bite.
AUTHOR: Bitterman-Deutsch O; Bergman R; Friedman-Birnbaum R
CORPORATE SOURCE: Dept. of Dermatology, Rambam Medical Center, Haifa.
SOURCE: HAREFUAH, (1990 Sep) 119 (5-6) 137-9.
Journal code: FZF; 0034351. ISSN: 0017-7768.
PUB. COUNTRY: Israel
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Hebrew
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199012
ENTRY DATE: Entered STN: 19910208
Last Updated on STN: 19910208
Entered Medline: 19901219

AB The diagnosis of bite by the brown recluse **spider**, Loxosceles reclusus, is rarely based on absolute identification of the insect because the victims are usually bitten while sleeping or dressing. More often, the history, clinical findings and course of the bite lead to the diagnosis. For early confirmation up to 24 hours after the bite, the passive hemagglutination test can be used. For older lesions, the in-vitro lymphocyte transformation test is useful, but is available in only a few medical centers. **Treatment** of the bite of the brown recluse **spider** varies from conservative to more active approaches.

Resting, local cooling, systemic antibiotics to prevent infection and mild anti-inflammatory drugs may be given. In the more active approach oral **corticosteroids** are added in the first 72 hours to the antibiotics, especially in massive bites with necrotic centers greater than 2 cm in diameter, or when there is systemic loxoscelism. Recently, good results have been reported with Avlosulfon (dapsone), which is claimed to cure necrotic cutaneous ulcerations, presumably by reducing the activity of polymorphonuclear leukocytes. Other **treatments** include specific antivenin, (of limited use because it must be administered shortly after the bite), and surgery to prevent spreading of the **venom**. We describe 3 cases of brown **spider** bite with typical clinical presentations in adults aged 20-40 years. 2 were **treated** with **corticosteroids** and antibiotics and 1 with Avlosulfon and prednisone, all within 72 hours of the bite. 2 recovered completely within a few days, but the third **treated** with prednisone and antibiotics, developed an ulcer which healed only after several months of **treatment**.(ABSTRACT TRUNCATED AT 250 WORDS)

L37 ANSWER 3 OF 5 MEDLINE
ACCESSION NUMBER: 89313407 MEDLINE
DOCUMENT NUMBER: 89313407 PubMed ID: 2664428
TITLE: Acute arthropod envenomation. Incidence, clinical features and management.
AUTHOR: Binder L S
CORPORATE SOURCE: Division of Emergency Medicine, Texas Tech University Regional Academic Health Center, El Paso.
SOURCE: MEDICAL TOXICOLOGY AND ADVERSE DRUG EXPERIENCE, (1989 May-Jun) 4 (3) 163-73. Ref: 84
Journal code: MTD; 8709214. ISSN: 0112-5966.
PUB. COUNTRY: New Zealand
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198908
ENTRY DATE: Entered STN: 19900309
Last Updated on STN: 19900309
Entered Medline: 19890825

AB Black widow **spider** (Latrodectus mactans) **envenomation** is found throughout both the temperate and tropical latitudes, and is one of the leading causes of death from arthropod **envenomations** worldwide. The **venom** is highly neurotoxic, affecting the presynaptic motor endplate to allow massive noradrenaline (norepinephrine) and acetylcholine release into synapses causing excessive stimulation and fatigue of the motor end plate and muscle. Clinically, patients develop a bite site lesion and pain, abdominal pain and tenderness, and lower extremity pain and weakness within minutes to hours of **envenomation**. Symptoms progress over several hours, then subside over 2 to 3 days. The recommended **treatment** of 'common' **envenomation** is calcium gluconate 10% intravenously, titrated to relief of symptoms; antivenin, although effective, may cause hypersensitivity and serum sickness reactions, and should be restricted to life-threatening **envenomations** only. Brown recluse **spider** (Loxosceles reclusa) **envenomations** are seen in the Americas and in Europe, and are endemic to the south and central United States. The **venom** contains at least 8 enzymes, consisting of various lysins (facilitating **venom** spread) and sphingomyelinase D, which causes cell membrane injury and lysis, thrombosis, local ischaemia, and chemotaxis. Local **envenomations** begin as pain and itching that progresses to vesiculation with violaceous necrosis and surrounding erythema, and ultimately ulcer formation. Systemic **envenomations** may be life threatening, and present with fever, constitutional symptoms, petechial eruptions, thrombocytopenia, and haemolysis with haemoglobinuric renal failure. **Treatment** of local **envenomations** is conservative (local wound care, cryotherapy, elevation, tetanus prophylaxis, and close follow-up); systemic **envenomation** requires supportive care and **treatment** of arising complications, **corticosteroids** to stabilise red blood cell membranes, and support of renal function. Dapsone 100mg daily has emerged as a promising **therapeutic** agent in both animal studies and clinical trials. Over 650 species of scorpions are known to cause **envenomation** (mostly in children under 10 years);

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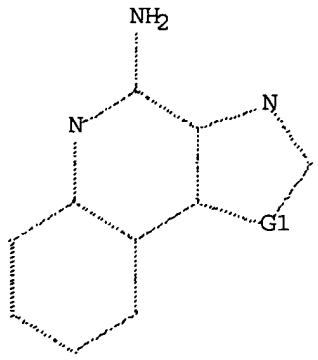

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INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
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L11      19621 ?VENOM?

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L12          1 L10 (S) L11

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L12  ANSWER 1 OF 1  HCAPLUS  COPYRIGHT 2001 ACS
AN   2001:747592  HCAPLUS
DN   135:268686
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TI Method for the treatment of dermal lesions caused by envenomation
IN Slade, Herbert B.
PA 3m Innovative Properties Company, USA
SO PCT Int. Appl., 14 pp.
    CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001074343	A2	20011011	WO 2001-US10291	20010330

        W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH,
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            KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX,
            MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM,
            TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD,
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OS MARPAT 135:268686

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            1 256922-47-1/BI
                (256922-47-1/RN)
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                (99011-02-6/RN)
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L13 ANSWER 1 OF 6 REGISTRY COPYRIGHT 2001 ACS
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OTHER NAMES:
CN 2-Butylthiazolo[4,5-c]quinolin-4-amine
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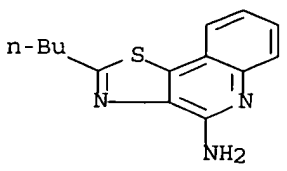
LC STN Files: CA, CAPLUS, TOXCENTER, TOXLIT, USPATFULL



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L13 ANSWER 2 OF 6 REGISTRY COPYRIGHT 2001 ACS
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CN 2-Propylthiazolo[4,5-c]quinolin-4-amine
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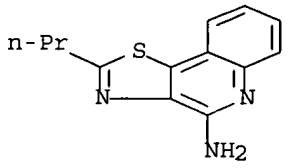

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2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L13 ANSWER 3 OF 6 REGISTRY COPYRIGHT 2001 ACS
RN **256922-51-7** REGISTRY
CN Thiazolo[4,5-c]quinolin-4-amine, 2-ethyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 2-Ethylthiazolo[4,5-c]quinolin-4-amine
MF C12 H11 N3 S
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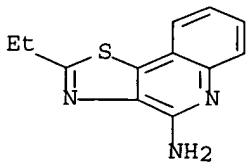
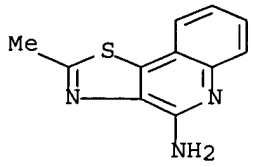
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, TOXLIT, USPATFULL



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

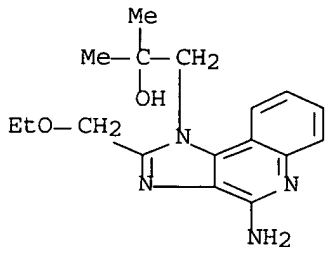
L13 ANSWER 4 OF 6 REGISTRY COPYRIGHT 2001 ACS
RN **256922-47-1** REGISTRY
CN Thiazolo[4,5-c]quinolin-4-amine, 2-methyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 2-Methylthiazolo[4,5-c]quinolin-4-amine
MF C11 H9 N3 S
CI COM
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, TOXLIT, USPATFULL



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

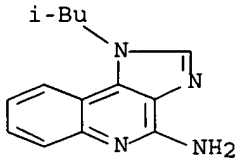
L13 ANSWER 5 OF 6 REGISTRY COPYRIGHT 2001 ACS
RN **144875-48-9** REGISTRY
CN 1H-Imidazo[4,5-c]quinoline-1-ethanol, 4-amino-2-(ethoxymethyl)-.alpha.,.alpha.-dimethyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 4-Amino-2-ethoxymethyl-.alpha.,.alpha.-dimethyl-1H-imidazo[4,5-c]quinoline-1-ethanol
CN R 848
CN Resiquimod
CN S 28463
DR 171742-32-8, 208711-44-8
MF C17 H22 N4 O2
SR CA
LC STN Files: ADISINSIGHT, ADISNEWS, BIOSIS, BIOTECHNO, CA, CAPLUS, CIN, DRUGNL, DRUGPAT, DRUGUPDATES, EMBASE, PHAR, SYNTHLINE, TOXCENTER, TOXLIT, USPATFULL



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

31 REFERENCES IN FILE CA (1967 TO DATE)
31 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L13 ANSWER 6 OF 6 REGISTRY COPYRIGHT 2001 ACS
RN **99011-02-6** REGISTRY
CN 1H-Imidazo[4,5-c]quinolin-4-amine, 1-(2-methylpropyl)- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Aldara
CN Imiquimod
CN R 837
CN S 26308
MF C14 H16 N4
CI COM
SR CA
LC STN Files: ADISINSIGHT, ADISNEWS, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CASREACT, CBNB, CIN, DDFU, DIOGENES, DRUGNL, DRUGPAT, DRUGU, DRUGUPDATES, EMBASE, IPA, MEDLINE, MRCK*, PHAR, PROMT, SYNTHLINE, TOXCENTER, TOXLIT, USAN, USPATFULL
(*File contains numerically searchable property data)
Other Sources: WHO



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

80 REFERENCES IN FILE CA (1967 TO DATE)
80 REFERENCES IN FILE CAPLUS (1967 TO DATE)

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=> fil medl capl biosis uspatf

=> s e6-11
L14         358 (144875-48-9/BI OR 256922-47-1/BI OR 256922-51-7/BI OR 256922-53
                -9/BI OR 256922-56-2/BI OR 99011-02-6/BI)

=> dup rem l14;
PROCESSING COMPLETED FOR L14
L15          248 DUP REM L14 (110 DUPLICATES REMOVED)


  IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> s ?immun?
   1 FILES SEARCHED...
   3 FILES SEARCHED...
L16     3762735 ?IMMUN?

=> s l16 and l15
L17         182 L16 AND L15

=> s l11 (s) l16
L18        6743 L11 (S) L16

=> s treat? or therap? or inbit?
   3 FILES SEARCHED...
L19     8537843 TREAT? OR THERAP? OR INBIT?

=> s spider? or jellyfish
L20       41321 SPIDER? OR JELLYFISH

=> s l20 (s) l18
L21         215 L20 (S) L18

=> s l19 (s) l21
L22          51 L19 (S) L21

=> focus
PROCESSING COMPLETED FOR L22
L23           51 FOCUS L22 1-

=> d ibib abs kwic 1-5

L23  ANSWER 1 OF 51  USPATFULL
ACCESSION NUMBER:       1999:58912  USPATFULL
TITLE:                  Treatment with polyvalent antivenom containing
                        immunoglobulin which is greater than 50% venom-reactive
INVENTOR(S):            Carroll, Sean B., Cottage Grove, WI, United States
PATENT ASSIGNEE(S):     Ophidian Pharmaceuticals, Inc., Madison, WI, United
                        States (U.S. corporation)

                             NUMBER       KIND    DATE
```

PATENT INFORMATION:	US 5904922	19990518
APPLICATION INFO.:	US 1995-442000	19950516 (8)
RELATED APPLN. INFO.:	Division of Ser. No. US 1994-275304, filed on 14 Jul 1994, now patented, Pat. No. US 5443976 which is a continuation of Ser. No. US 1992-983668, filed on 1 Dec 1992, now abandoned which is a division of Ser. No. US 1989-429791, filed on 31 Oct 1989, now patented, Pat. No. US 5196193	
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	Granted	
PRIMARY EXAMINER:	Naff, David M.	
LEGAL REPRESENTATIVE:	Medlen & Carroll, LLP	
NUMBER OF CLAIMS:	12	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	18 Drawing Figure(s); 16 Drawing Page(s)	
LINE COUNT:	3895	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB **Antivenoms** to snake, **spider**, scorpion and jelly fish **venoms** are produced for **treatment** of humans and animals, and for analytical use. Polyvalent **antivenoms** are produced containing **immunoglobulin** which is greater than fifty percent **venom** reactive. Purified polyvalent **antivenom** is derived from a first polyvalent **antivenom** having two or more monovalent subpopulations, and purified such that greater than fifty percent of the monovalent subpopulations are recovered by weight. The **antivenoms** can be horse or avian such as chicken **antivenom**. Chicken **antivenom** is obtained using a whole **venom** that is not glutaraldehyde pretreated, and the **antivenom** contains yolk **immunoglobulin**. **Antivenoms** are purified with an antigen matrix containing a single whole **venom** or a plurality of whole **venoms** covalently attached to an insoluble support such as aldehyde-activated agarose. Preferably, the whole **venoms** forming the plurality of whole **venoms** are selected from the four whole **venoms** of C. atrox, B. atrox, C. adamanteus and C. durissus terrificus. A combination of immobilized C. atrox and C. durissus terrificus whole **venoms** can substantially purify **antivenom** reactive with all four **venoms**. The **antivenoms** are intravenously injected to **treat** an **envenomed** mammalian subject.

L23 ANSWER 2 OF 51 MEDLINE

ACCESSION NUMBER:	1999368799 MEDLINE
DOCUMENT NUMBER:	99368799 PubMed ID: 10439926
TITLE:	Antivenom therapy in the Americas.
AUTHOR:	Heard K; O'Malley G F; Dart R C
CORPORATE SOURCE:	Rocky Mountain Poison and Drug Center, Denver, Colorado, USA.
SOURCE:	DRUGS, (1999 Jul) 58 (1) 5-15. Ref: 62 Journal code: EC2; 7600076. ISSN: 0012-6667.
PUB. COUNTRY:	New Zealand
	Journal; Article; (JOURNAL ARTICLE)
	General Review; (REVIEW)
	(REVIEW, TUTORIAL)
LANGUAGE:	English
FILE SEGMENT:	Priority Journals
ENTRY MONTH:	199910
ENTRY DATE:	Entered STN: 19991014
	Last Updated on STN: 19991014
	Entered Medline: 19991004

AB **Envenomations** are an important cause of injury in the Americas. While supportive care alone may result in an acceptable outcome, **antivenom** offers a specific **therapy** that can significantly reduce the injury and symptoms of the **envenomation** . **Antivenoms** are **hyperimmune** sera collected from animals **immunised** with **venom**. The antibodies contained in the serum bind and inactive **venom** components. This leads to cessation or reversal of the toxic effects of the **venom**. The serum is often processed to increase the level of antibodies directed against **venom** components and decrease the amount of inactive proteins that may cause allergic reactions. The processing may include precipitation of inactive proteins, chromatographic methods and cleavage

of the **immunoglobulins** to form antibody fragments known as Fab or F(ab)2. In the Americas, **antivenoms** are produced to **treat** crotalid and Micrurus snake **envenomations**. Latrodectus and Loxosceles **spider envenomations** and Centruroides and Tityus scorpion **envenomations**. The indications, method of administration and incidence of adverse reactions differ greatly for each **antivenom**. The adverse effects encountered when using **antivenoms** are primarily allergic in nature. Anaphylaxis, which may be life threatening, is a major concern. Preparations to **treat** anaphylaxis must be made before initiating **antivenom** **therapy**. Serum sickness is also common with many of the **antivenom** preparations.

L23 ANSWER 3 OF 51 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 2000:395043 BIOSIS
DOCUMENT NUMBER: PREV200000395043
TITLE: Anti-lethal factor from opossum serum is a potent antidote for animal, plant and bacterial toxins.
AUTHOR(S): Lipps, B. V. (1)
CORPORATE SOURCE: (1) Ophidia Products Inc., 11320 South Post Oak, Suite 203, Houston, TX, 77035 USA
SOURCE: Journal of Venomous Animals and Toxins, (1999) Vol. 5, No. 1 CITED APRIL 17, 2000, pp. 1-16. http://www.scielo.br/cgi-bin/fbpe/fbtext?got=last&pid=S0104-79301999000100005&usr=fbpe&lng=en&seq=01 cited May 9, 2000 http://www.scielo.br/cgi-bin/fbpe/fball?got=all&pid=0104-7930&usr=fbpe&lng=en&nrm=iso&sss=1&aut=71981947. online. ISSN: 0104-7930.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Currently, the use of **antivenoms** is the only available **treatment** for **envenomation** caused by **venomous** animals namely, snake, scorpion, **spider**, tick and jelly fish. **Antivenoms** are generally produced in large animals, mostly in horses. A large percentage of the population is allergic to horse proteins. Several animals are known to be resistant to snakebites and the antihemorrhagic and anti-lethal components have been isolated from sera of opossum, mongoose, meerkat and hedgehog, as well as from **venomous** and non-**venomous** snakes. Anti-lethal factor named Lethal Toxin Neutralizing Factor (LTNF) has been isolated in purity from opossum (Didelphis virginiana) serum by high pressure liquid chromatography (HPLC). The molecular weight of LTNF is 63 kDa, and it does not form precipitation with **venoms** or toxins by **immunodiffusion** . Death due to intraperitoneal (IP) injection of a predetermined lethal dose of **venom** from major families of snakes, for instance Crotalidae, Elapidae, Viperidae and Hydrophiidae, is prevented in mice by subsequent IP inoculation of LTNF. Furthermore, LTNF neutralizes the lethality of scorpion and bee **venoms** and toxins from various animals, plants and bacteria. Thus, natural LTNF from opossum serum has potential as a universal **therapy** for **envenomation** caused by animals, plants and bacteria.

L23 ANSWER 4 OF 51 MEDLINE
ACCESSION NUMBER: 96431938 MEDLINE
DOCUMENT NUMBER: 96431938 PubMed ID: 8835004
TITLE: [Case report of jellyfish injury]. Fallstudie einer Quallenverletzung.
AUTHOR: Raupp U; Milde P; Goerz G; Plewig G; Burnett J; Heeger T
CORPORATE SOURCE: Hautklinik, Heinrich-Heine-Universitat, Dusseldorf.
SOURCE: HAUTARZT, (1996 Jan) 47 (1) 47-52. Journal code: G13; 0372755. ISSN: 0017-8470.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: German
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199612
ENTRY DATE: Entered STN: 19970128
Last Updated on STN: 19970128
Entered Medline: 19961204
AB We are presenting a 47-year-old woman who was stung by **jellyfish** while bathing in the sea of Thailand. Immediately after the injury she developed sharp pain and urticarial erythema of the skin of the knees

accompanied by muscle cramps of the entire body. After a few days a toxic contact dermatitis with edematous swelling and ulcerations developed, which did not respond to topical antibiotics or corticosteroids. Three weeks later the patient presented with a disseminated urticarial eruption, which at first responded well to topical **treatment** and systemic corticosteroids. Over the next few weeks, however, a relapse of the eruption and the ulcerations occurred. Raised titres of IgG and IgM antibodies against different **jellyfish** from the Indian and Pacific Ocean were detected in the patient's serum by the enzyme-linked **immunosorbent** assay. Antibodies against bees (class 1) and wasps (class 4) were found by the radioallergosorbent test. The clinical features and the **immunological** findings led to the diagnosis of toxic and allergic contact dermatitis to **jellyfish venom** . First aid and secondary **treatment** of **jellyfish** injuries are suggested.

L23 ANSWER 5 OF 51 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1996:164485 BIOSIS
DOCUMENT NUMBER: PREV199698736620
TITLE: Case study of a jellyfish injury.
AUTHOR(S): Raupp, Ulrike; Milde, Petra; Goerz, Guenter (1); Plewig, Gerd; Burnett, Joseph; Heeger, Thomas
CORPORATE SOURCE: (1) Univ.-Hautklinik, Moorenstrasse 5, D-40225 Duesseldorf Germany
SOURCE: Hautarzt, (1996) Vol. 47, No. 1, pp. 47-52.
ISSN: 0017-8470.
DOCUMENT TYPE: Article
LANGUAGE: German
SUMMARY LANGUAGE: German; English
AB We are presenting a 47-year-old woman who was stung by **jellyfish** while bathing in the sea of Thailand. Immediately after the injury she developed sharp pain and urticarial erythema of the skin of the knees accompanied by muscle cramps of the entire body. After a few days a toxic contact dermatitis with edematous swelling and ulcerations developed, which did not respond to topical antibiotics or corticosteroids. Three weeks later the patient presented with a disseminated urticarial eruption, which at first responded well to topical **treatment** and systemic corticosteroids. Over the next few weeks, however, a relapse of the eruption and the ulcerations occurred. Raised titres of IgG and IgM antibodies against different **jellyfish** from the Indian and Pacific Ocean were detected in the patient's serum by the enzyme-linked **immunosorbent** assay. Antibodies against bees (class 1) and wasps (class 4) were found by the radioallergosorbent test. The clinical features and the **immunological** findings led to the diagnosis of toxic and allergic contact dermatitis to **jellyfish venom** . First aid and secondary **treatment** of **jellyfish** injuries are suggested.

=> d his

(FILE 'HOME' ENTERED AT 17:06:53 ON 27 DEC 2001)

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L1 1 S ZIPRASIDONE/CN

FILE 'CAPLUS' ENTERED AT 17:07:18 ON 27 DEC 2001

FILE 'REGISTRY' ENTERED AT 17:07:27 ON 27 DEC 2001
SEL NAME L1 1

FILE 'HCAPLUS' ENTERED AT 17:07:50 ON 27 DEC 2001
L2 169 S E1-5 OR L1
L3 93 S L1 AND THU/RL
L4 186327 S ?OBES? OR WEIGHT LOSS OR WEIGHT GAIN OR OVERWEIG?
L5 11 S L3 (S) L4
L6 11 FOCUS L5 1-

FILE 'REGISTRY' ENTERED AT 17:51:23 ON 27 DEC 2001
L7 STRUCTURE UPLOADED
L8 50 S L7
L9 1291 S L7 FULL

FILE 'HCAPLUS' ENTERED AT 17:52:23 ON 27 DEC 2001

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L10         125 S L9
L11       19621 S ?VENOM?
L12           1 S L10 (S) L11
                SEL RN L12 1

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L13           6 S E6-11

     FILE 'CAPLUS' ENTERED AT 17:53:34 ON 27 DEC 2001

     FILE 'MEDLINE, CAPLUS, BIOSIS, USPATFULL' ENTERED AT 17:53:42 ON 27 DEC
     2001
L14         358 S E6-11
L15         248 DUP REM L14 (110 DUPLICATES REMOVED)
L16     3762735 S ?IMMUN?
L17         182 S L16 AND L15
L18        6743 S L11 (S) L16
L19     8537843 S TREAT? OR THERAP? OR INBIT?
L20       41321 S SPIDER? OR JELLYFISH
L21         215 S L20 (S) L18
L22          51 S L19 (S) L21
L23          51 FOCUS L22 1-

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PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L11 (S) L66'
L24          1 L11 (S) L15

=> s l11 and l15
L25          1 L11 AND L15

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PROCESSING COMPLETED FOR L23
L26          36 DUP REM L23 (15 DUPLICATES REMOVED)

=> d ibib abs kwic 1-5

L26  ANSWER 1 OF 36     MEDLINE
ACCESSION NUMBER:   2001693948     IN-PROCESS
DOCUMENT NUMBER:    21605843   PubMed ID: 11738237
TITLE:              Apoptosis induced by box jellyfish (Chiropsalmus
                    Quadrigatus) toxin in glioma and vascular endothelial cell
                    lines.
AUTHOR:             Sun Lian Kun; Yoshii Yoshihiko; Hyodo Akio; Tsurushima
                    Hideo; Saito Atsushi; Harakuni Tsuyoshi; Li Ya Ping; Nozaki
                    Masatoshi; Morine Nobuya
CORPORATE SOURCE:   Department of Neurosurgery, Faculty of Medicine, University
                    of the Ryukyus, Nishihara Uehara 207, 903-0215, Okinawa,
                    Japan.
SOURCE:             TOXICON, (2002 Apr) 40 (4) 441-6.
                    Journal code: VWT; 1307333. ISSN: 0041-0101.
PUB. COUNTRY:       England: United Kingdom
                    Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:           English
FILE SEGMENT:       IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE:         Entered STN: 20011217
                    Last Updated on STN: 20011217
AB   This study was made to investigate whether Chiropsalmus Quadrigatus toxins
     (CqTX), which isolated from box jellyfish C. Quadrigatus
     venom, could induce apoptosis in human U251 and rat C6 malignant
     glioma cells and transformed vascular endothelial ECV 304 cell lines. Cell
     viability was estimated by MTT assay. Apoptosis was evaluated using TdT
     (terminal deoxynucleotidyl transferase)-mediated dUTP nick-end labeling
     (TUNEL) method and DNA gel electrophoresis. Furthermore, the expression of
     p53 protein was examined immunohistochemically in the U251
     cells. After the CqTX treatment, the growth of all cell lines
     was inhibited, the fragmented DNA was observed and some cells became TUNEL
     positive. The expression of p53 protein was increased in the tested U251
     cells. The results suggested that CqTX induced apoptosis in these cell
     lines. The promotion of the p53 expression might be one mechanism of
     apoptosis induced by CqTX in the glioma cells.

L26  ANSWER 2 OF 36  CAPLUS  COPYRIGHT 2001 ACS
```

ACCESSION NUMBER: 2001:416998 CAPLUS
DOCUMENT NUMBER: 135:32739
TITLE: Immunogen, antivenom and vaccine against the venom of the black widow spider
INVENTOR(S): Gurrola Briones, Georgina; Alagon Cano, Alejandro; Possani Postay, Lourival Domingos; Grishin, Eugene Vasilevich; Lipkin, Alexei Valerevich; Volynski, Kirill Evgenevich
PATENT ASSIGNEE(S): Universidad Nacional Autonoma de Mexico, Mex.; Shemyakin and Ovchinnikov Institute of Bioorganic Chemistry
SOURCE: PCT Int. Appl., 59 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Spanish
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001040290	A1	20010607	WO 2000-MX48	20001128

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: MX 1999-11191 A 19991203

AB The invention relates to a recombinant polypeptide that comprises the N-terminal region of .alpha.-Latrotoxin, is capable of generating an immune response in mammals, and efficiently and fully neutralizes the venom of the black widow spider. The invention also relates to the cDNA coding for said polypeptide, the vector for the expression thereof, the bacterial cells transformed with said vector, and a method for producing the polypeptide by means of culture of said cells. The invention further relates to the use of said recombinant polypeptide as a vaccine against the venom of the black widow spider and to pharmaceutically prepns. of said vaccine. The invention addnl. relates to the use of said recombinant polypeptide as **immunogen** for generating **antivenom** serum for the black widow **spider**, obtaining serotherapeutic agents by serum purifn. and Fab **therapeutic** agents by enzymic hydrolysis of the antibodies of the serum. The invention also relates to an immunogen matrix that is useful in the sepn. and purifn. of antibodies and antibody fragments against the venom of the black widow spider.

REFERENCE COUNT: 3
REFERENCE(S): (1) British Tech Group; WO 9529235 A 1995 CAPLUS
(2) Grinshin, E; TOXICON 1998, V36(11), P1693
(3) Kiyatkin, N; FEBS LETTERS 1990, V270(1,2), P127

L26 ANSWER 3 OF 36 USPATFULL
ACCESSION NUMBER: 2000:174351 USPATFULL
TITLE: Representations of bimolecular interactions
INVENTOR(S): Gershoni, Jonathan M., Rehovot, Israel
Enshel, David, Givatayim, Israel
PATENT ASSIGNEE(S): Ramot University Authority for Applied Research & Industrial Development Ltd., Tel Aviv, Israel (non-U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6165722		20001226	
	WO 9820159		19980514	
APPLICATION INFO.:	US 1999-297669		19990506	(9)
	WO 1997-IL354		19971104	
			19990506	PCT 371 date
			19990506	PCT 102(e) date

	NUMBER	DATE
PRIORITY INFORMATION:	IL 1996-119587	19961107

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Jones, W. Gary
ASSISTANT EXAMINER: Forman, B J
LEGAL REPRESENTATIVE: Friedman, Mark M.
NUMBER OF CLAIMS: 34
EXEMPLARY CLAIM: 1
LINE COUNT: 1587
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A method of preparing a bimolecular interaction library for a first biological unit and for a second biological unit, each of the first and second biological units having a corresponding genetic material, the method comprising the steps of: (a) preparing a first fragment from the genetic material corresponding to the first biological unit; (b) preparing a first phage library having a first selection marker with the first fragment, such that a first peptide is displayed by the first phage library; (c) preparing a second fragment from the genetic material corresponding to the second biological unit; (d) preparing a second phage library having a second selection marker with the second fragment, such that a second peptide is displayed by the second phage library; (e) mixing the first phage library and the second phage library; and (f) co-selecting co-selected phages from the first phage library and from the second phage library by the first selection marker and the second selection marker when a selection process yields a positive result, such that the selection process yields the positive result only when the first peptide and the second peptide interact, and such that the bimolecular interaction library is formed from the co-selected phages.

L26 ANSWER 4 OF 36 USPATFULL
ACCESSION NUMBER: 2000:12973 USPATFULL
TITLE: Cytoprotective compounds
INVENTOR(S): Franson, Richard C., Richmond, VA, United States
Ottenbrite, Raphael M., Midlothian, VA, United States
PATENT ASSIGNEE(S): Virginia Commonwealth University, Richmond, VA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6020510		20000201
APPLICATION INFO.:	US 1998-17511		19980202 (9)

RELATED APPLN. INFO.: Continuation of Ser. No. US 1996-632030, filed on 15 Apr 1996, now patented, Pat. No. US 5859271
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Reamer, James H.
LEGAL REPRESENTATIVE: Jones & Askew LLP
NUMBER OF CLAIMS: 31
EXEMPLARY CLAIM: 1
LINE COUNT: 1891
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention provides compositions and methods for protecting cells from injury due to intrinsic membrane lysis, oxidation and/or invasion by destructive agents. Even more particularly, the present invention provides compositions and methods for treating or prophylactically inhibiting phospholipase mediated injury, injury due to oxidation, and inflammation. In a very specific sense, this invention provides compositions and methods of making these compositions that are inhibitors of phospholipase.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM Another object of the present invention is to provide oral and topical **treatments** comprising administration of an effective amount of the compositions of the present invention, for a variety of conditions, such conditions. . . . including septic shock, anaphylactic shock, anaphylactic shock resulting from radiocontrast administration, and shock resulting from bacterial infections; bacterial infections; uremia; **autoimmune** disorders; parasitic infections including, but not limited to, malaria; inflammation including allergic inflammation; skin inflammation, itching, and other dermatologic disorders. . . . poison ivy, poison oak, poison sumac; bites of insects including, but not limited to, mosquitos, fire ants, chiggers, ticks, bees, **spiders**, fleas and flies; bites of reptiles, especially **venomous**

reptiles, amphibians, and other animals; contact with various animals with **venom** on their skin such as poisonous frogs; pruritis associated with local dermatologic or systemic disease; prevention of tissue ischemia including. . .

L26 ANSWER 5 OF 36 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 2000158515 MEDLINE
DOCUMENT NUMBER: 20158515 PubMed ID: 10695968
TITLE: Identification of high molecular weight serine-proteases in Loxosceles intermedia (brown spider) venom.
AUTHOR: Veiga S S; da Silveira R B; Dreyfus J L; Haoach J; Pereira A M; Mangili O C; Gremski W
CORPORATE SOURCE: Department of Cell Biology, Federal University of Parana, Curitiba, Brazil.. veigass@bio.ufpr.br
SOURCE: TOXICON, (2000 Jun) 38 (6) 825-39.
Journal code: VWT; 1307333. ISSN: 0041-0101.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200004
ENTRY DATE: Entered STN: 20000421
Last Updated on STN: 20000421
Entered Medline: 20000412

AB High molecular weight serine-proteases have been identified in Loxosceles intermedia (brown **spider**) **venom**. The mechanism by which Loxosceles spp **venoms** cause dermonecrotic injury (a hallmark of loxoscelism) is currently under investigation, but it seems to be molecularly complex and in some instance proteases might be expected to play a role in this skin lesion. In the present investigation, when we submitted L. intermedia **venom** to linear gradient 3-20% SDS-PAGE stained by a monochromatic silver method we detected a heterogeneous protein profile in molecular weight, ranging from 850- to 5-kDa. In an attempt to detect zymogen molecules of proteolytic enzymes, **venom** aliquots were **treated** with several exogenous proteases. Among them, trypsin activated two gelatinolytic molecules of 85- and 95-kDa in the **venom**. In experiments of hydrolysis inactivation using different protease inhibitors for four major class of proteases, we detected that only serine-type protease inhibitors were able to inactivate the 85- and 95-kDa enzymes in the **venom**. An examination of the 85- and 95-kDa gelatinolytic activities as a function of pH showed that these proteases had no apparent activities at pH below 5.0 and higher than 9.0 and displayed little activity at pH 6.0. with the optimal pH for their activities ranging from 7.0 to 8.0. Evaluation of the functional specificities of the 85- and 95-kDa **venom** proteases showed that these proteases efficiently degrade gelatin (denatured collagen) but have no proteolytic activity on hemoglobin, **immunoglobulin**, albumin, librinogen or laminin, suggesting specificity of their proteolytic actions. We describe here two serine-proteases activities in L. intermedia **venom** probably involved in the harmful effects of the **venom**.

=> focus
PROCESSING COMPLETED FOR L26
L27 36 FOCUS L26 1-

=> d ibib abs kwic 1-10

L27 ANSWER 1 OF 36 USPATFULL
ACCESSION NUMBER: 1999:58912 USPATFULL
TITLE: Treatment with polyvalent antivenom containing immunoglobulin which is greater than 50% venom-reactive
INVENTOR(S): Carroll, Sean B., Cottage Grove, WI, United States
PATENT ASSIGNEE(S): Ophidian Pharmaceuticals, Inc., Madison, WI, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5904922		19990518
APPLICATION INFO.:	US 1995-442000		19950516 (8)

RELATED APPLN. INFO.: Division of Ser. No. US 1994-275304, filed on 14 Jul 1994, now patented, Pat. No. US 5443976 which is a continuation of Ser. No. US 1992-983668, filed on 1 Dec

1992, now abandoned which is a division of Ser. No. US 1989-429791, filed on 31 Oct 1989, now patented, Pat. No. US 5196193
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Naff, David M.
LEGAL REPRESENTATIVE: Medlen & Carroll, LLP
NUMBER OF CLAIMS: 12
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 18 Drawing Figure(s); 16 Drawing Page(s)
LINE COUNT: 3895
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB **Antivenoms** to snake, **spider**, scorpion and jelly fish **venoms** are produced for **treatment** of humans and animals, and for analytical use. Polyvalent **antivenoms** are produced containing **immunoglobulin** which is greater than fifty percent **venom** reactive. Purified polyvalent **antivenom** is derived from a first polyvalent **antivenom** having two or more monovalent subpopulations, and purified such that greater than fifty percent of the monovalent subpopulations are recovered by weight. The **antivenoms** can be horse or avian such as chicken **antivenom**. Chicken **antivenom** is obtained using a whole **venom** that is not glutaraldehyde pretreated, and the **antivenom** contains yolk **immunoglobulin**. **Antivenoms** are purified with an antigen matrix containing a single whole **venom** or a plurality of whole **venoms** covalently attached to an insoluble support such as aldehyde-activated agarose. Preferably, the whole **venoms** forming the plurality of whole **venoms** are selected from the four whole **venoms** of C. atrox, B. atrox, C. adamanteus and C. durissus terrificus. A combination of immobilized C. atrox and C. durissus terrificus whole **venoms** can substantially purify **antivenom** reactive with all four **venoms**. The **antivenoms** are intravenously injected to **treat** an **envenomed** mammalian subject.

L27 ANSWER 2 OF 36 MEDLINE
ACCESSION NUMBER: 1999368799 MEDLINE
DOCUMENT NUMBER: 99368799 PubMed ID: 10439926
TITLE: Antivenom therapy in the Americas.
AUTHOR: Heard K; O'Malley G F; Dart R C
CORPORATE SOURCE: Rocky Mountain Poison and Drug Center, Denver, Colorado, USA.
SOURCE: DRUGS, (1999 Jul) 58 (1) 5-15. Ref: 62
Journal code: EC2; 7600076. ISSN: 0012-6667.
PUB. COUNTRY: New Zealand
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199910
ENTRY DATE: Entered STN: 19991014
Last Updated on STN: 19991014
Entered Medline: 19991004

AB **Envenomations** are an important cause of injury in the Americas. While supportive care alone may result in an acceptable outcome, **antivenom** offers a specific **therapy** that can significantly reduce the injury and symptoms of the **envenomation**. **Antivenoms** are **hyperimmune** sera collected from animals **immunised** with **venom**. The antibodies contained in the serum bind and inactive **venom** components. This leads to cessation or reversal of the toxic effects of the **venom**. The serum is often processed to increase the level of antibodies directed against **venom** components and decrease the amount of inactive proteins that may cause allergic reactions. The processing may include precipitation of inactive proteins, chromatographic methods and cleavage of the **immunoglobulins** to form antibody fragments known as Fab or F(ab)2. In the Americas, **antivenoms** are produced to **treat** crotalid and Micrurus snake **envenomations**. Latrodectus and Loxosceles **spider envenomations** and Centruroides and Tityus scorpion **envenomations**. The indications,

method of administration and incidence of adverse reactions differ greatly for each **antivenom**. The adverse effects encountered when using **antivenoms** are primarily allergic in nature. Anaphylaxis, which may be life threatening, is a major concern. Preparations to **treat** anaphylaxis must be made before initiating **antivenom** **therapy**. Serum sickness is also common with many of the **antivenom** preparations.

L27 ANSWER 3 OF 36 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 2000:395043 BIOSIS
DOCUMENT NUMBER: PREV200000395043
TITLE: Anti-lethal factor from opossum serum is a potent antidote for animal, plant and bacterial toxins.
AUTHOR(S): Lipps, B. V. (1)
CORPORATE SOURCE: (1) Ophidia Products Inc., 11320 South Post Oak, Suite 203, Houston, TX, 77035 USA
SOURCE: Journal of Venomous Animals and Toxins, (1999) Vol. 5, No. 1 CITED APRIL 17, 2000, pp. 1-16. http://www.scielo.br/cgi-bin/fbpe/fbtext?got=last&pid=S0104-79301999000100005&usr=fbpe&lng=en&seq=01 cited May 9, 2000 http://www.scielo.br/cgi-bin/fbpe/fball?got=all&pid=0104-7930&usr=fbpe&lng=en&nrm=iso&sss=1&aut=71981947. online. ISSN: 0104-7930.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Currently, the use of **antivenoms** is the only available **treatment** for **envenomation** caused by **venomous** animals namely, snake, scorpion, **spider**, tick and jelly fish. **Antivenoms** are generally produced in large animals, mostly in horses. A large percentage of the population is allergic to horse proteins. Several animals are known to be resistant to snakebites and the antihemorrhagic and anti-lethal components have been isolated from sera of opossum, mongoose, meerkat and hedgehog, as well as from **venomous** and non-**venomous** snakes. Anti-lethal factor named Lethal Toxin Neutralizing Factor (LTNF) has been isolated in purity from opossum (Didelphis virginiana) serum by high pressure liquid chromatography (HPLC). The molecular weight of LTNF is 63 kDa, and it does not form precipitation with **venoms** or toxins by **immunodiffusion** . Death due to intraperitoneal (IP) injection of a predetermined lethal dose of **venom** from major families of snakes, for instance Crotalidae, Elapidae, Viperidae and Hydrophiidae, is prevented in mice by subsequent IP inoculation of LTNF. Furthermore, LTNF neutralizes the lethality of scorpion and bee **venoms** and toxins from various animals, plants and bacteria. Thus, natural LTNF from opossum serum has potential as a universal **therapy** for **envenomation** caused by animals, plants and bacteria.

L27 ANSWER 4 OF 36 MEDLINE
ACCESSION NUMBER: 96431938 MEDLINE
DOCUMENT NUMBER: 96431938 PubMed ID: 8835004
TITLE: [Case report of jellyfish injury]. Fallstudie einer Quallenverletzung.
AUTHOR: Raupp U; Milde P; Goerz G; Plewig G; Burnett J; Heeger T
CORPORATE SOURCE: Hautklinik, Heinrich-Heine-Universitat, Dusseldorf.
SOURCE: HAUTARZT, (1996 Jan) 47 (1) 47-52. Journal code: G13; 0372755. ISSN: 0017-8470.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: German
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199612
ENTRY DATE: Entered STN: 19970128 Last Updated on STN: 19970128 Entered Medline: 19961204
AB We are presenting a 47-year-old woman who was stung by **jellyfish** while bathing in the sea of Thailand. Immediately after the injury she developed sharp pain and urticarial erythema of the skin of the knees accompanied by muscle cramps of the entire body. After a few days a toxic contact dermatitis with edematous swelling and ulcerations developed, which did not respond to topical antibiotics or corticosteroids. Three weeks later the patient presented with a disseminated urticarial eruption, which at first responded well to topical **treatment** and systemic

corticosteroids. Over the next few weeks, however, a relapse of the eruption and the ulcerations occurred. Raised titres of IgG and IgM antibodies against different **jellyfish** from the Indian and Pacific Ocean were detected in the patient's serum by the enzyme-linked **immunosorbent** assay. Antibodies against bees (class 1) and wasps (class 4) were found by the radioallergosorbent test. The clinical features and the **immunological** findings led to the diagnosis of toxic and allergic contact dermatitis to **jellyfish venom** . First aid and secondary **treatment** of **jellyfish** injuries are suggested.

L27 ANSWER 5 OF 36 MEDLINE
ACCESSION NUMBER: 83224902 MEDLINE
DOCUMENT NUMBER: 83224902 PubMed ID: 6407159
TITLE: Incompatibility associated with the bite of a brown recluse spider (Loxosceles reclusa).
AUTHOR: Hardman J T; Beck M L; Hardman P K; Stout L C
SOURCE: TRANSFUSION, (1983 May-Jun) 23 (3) 233-6.
Journal code: WDN; 0417360. ISSN: 0041-1132.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198307
ENTRY DATE: Entered STN: 19900319
Last Updated on STN: 19980206
Entered Medline: 19830708

AB Red cell samples from a patient who was suffering from massive hemolysis due to a brown recluse **spider** (Loxosceles reclusa) bite were found to be reactive by indirect antiglobulin test with most ABO-compatible serum samples. **Spider venom**, enzymes related to those in **spider venom**, and antisera to plasma proteins and Rh antigens were used to investigate the unusual reactivity of the patient's cells. IgG was detected on the patient's cells by indirect antiglobulin tests. Cells **treated** with brown recluse **spider venom** or phosphatidylcholine phosphatidohydrolase reacted similarly. These findings suggest that sphingomyelinase D, which has been identified in brown recluse **spider venom**, may be related to the unusual reactivity of the patient's cells. Unexpected reactions were observed when **venom-treated** cells were tested with Rh antibodies: O negative cells absorbed and eluted anti-D from Rh **immune** globulin; E negative cells were reactive with a commercial anti-E reagent.

L27 ANSWER 6 OF 36 MEDLINE
ACCESSION NUMBER: 97380568 MEDLINE
DOCUMENT NUMBER: 97380568 PubMed ID: 9237343
TITLE: Antigenic cross-reactivity of venoms from medically important Loxosceles (Araneae) species in Brazil.
AUTHOR: Barbaro K C; Eickstedt V R; Mota I
CORPORATE SOURCE: Laboratorio de Imunopatologia, Instituto Butantan, Sao Paulo, Brazil.
SOURCE: TOXICON, (1994 Jan) 32 (1) 113-20.
Journal code: VWT; 1307333. ISSN: 0041-0101.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199708
ENTRY DATE: Entered STN: 19970908
Last Updated on STN: 19970908
Entered Medline: 19970826

AB Antigenic cross-reactivity between the components of **venoms** from three **spiders** of the genus Loxosceles, L. gaucho, L. laeta and L. intermedia, was studied. Species-specific antisera were prepared by **immunization** of rabbits with each **venom**. Anti-L. gaucho horse **hyperimmune** serum provided by the Butantan Institute for **treatment** of accidents with these **spiders** was also used. Separation by SDS-PAGE showed the existence of many common components in the three antigens. No individual antigen was observed. Analysis of the antisera by ELISA and Western blotting showed cross-reactivity as well as several common bands between the three **venoms**. The horse anti-L. gaucho **venom** serum recognized many common proteins when antigens

of the other two species were used. Antigens in the range of 33,000-35,000 mol. wt showed most cross-reactivity. Both horse and rabbit anti-**venom** sera contained antibodies able to neutralize the lethal and dermonecrotic activities of the **venom** of the three species studied.

L27 ANSWER 7 OF 36 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1980:635458 CAPLUS
DOCUMENT NUMBER: 93:235458
TITLE: The utilization of the bradykinin radioimmunoassay for the study of a kinin-like factor in jellyfish toxin
AUTHOR(S): Hartman, Karen R.; Calton, Gary J.; Burnett, Joseph W.
CORPORATE SOURCE: Div. Dermatol., Univ. Maryland Sch. Med., Baltimore, MD, 21201, USA
SOURCE: Comp. Biochem. Physiol. C (1980), 66C(2), 163-8
CODEN: CBPCBB; ISSN: 0306-4492
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A kinin-like factor was detected in **jellyfish** (sea nettle) nematocyst **venom**, using a std. bradykinin **radioimmunoassay** which was sensitive to salt concn. and pH, thus limiting the range of **treatments** which could be utilized to study the peptide. The peptide was thermolabile at 37.degree. and not concd. by (NH4)2SO4 pptn. SP-Sephadex, DEAE-Sephacel, and hydroxylapatite chromatog. increased sp. activity of the peptide. Trypsin, chymotrypsin, and carboxypeptidase B were ineffective against the kinin. The biochem. characteristics of bradykinin and the jellyfish kinin are compared.

L27 ANSWER 8 OF 36 MEDLINE
ACCESSION NUMBER: 2000137001 MEDLINE
DOCUMENT NUMBER: 20137001 PubMed ID: 10674536
TITLE: Green lynx spider (Peucetia viridans) envenomation.
AUTHOR: Bush S P; Giem P; Vetter R S
CORPORATE SOURCE: Department of Emergency Medicine, Loma Linda University School of Medicine, CA, USA.. famensean@aol.com
SOURCE: AMERICAN JOURNAL OF EMERGENCY MEDICINE, (2000 Jan) 18 (1) 64-6. Ref: 10
Journal code: AA2; 8309942. ISSN: 0735-6757.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW OF REPORTED CASES)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200002
ENTRY DATE: Entered STN: 20000309
Last Updated on STN: 20000309
Entered Medline: 20000224
AB Four cases of **envenomation** by green lynx **spiders** (Peucetia viridans) are reported. Despite the unusual appearance and occasional aggressive behavior of this **spider**, **envenomation** caused only local pain, pruritis, erythema, and induration. No local necrosis or systemic symptoms occurred. **Treatment** included tetanus **immunization**, wound care, and symptomatic **therapy**.

L27 ANSWER 9 OF 36 MEDLINE
ACCESSION NUMBER: 1999325879 MEDLINE
DOCUMENT NUMBER: 99325879 PubMed ID: 10400292
TITLE: Development and evaluation of the neutralizing capacity of horse antivenom against the Brazilian spider Loxosceles intermedia.
AUTHOR: Braz A; Minozzo J; Abreu J C; Gubert I C; Chavez-Olortegui C
CORPORATE SOURCE: Departamento de Patologia Basica, Setor de Ciencias Biologicas, Universidade Federal do Parana, Curitiba, Brasil.
SOURCE: TOXICON, (1999 Sep) 37 (9) 1323-8.
Journal code: VWT; 1307333. ISSN: 0041-0101.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals

ENTRY MONTH: 199909
ENTRY DATE: Entered STN: 19990913
Last Updated on STN: 19990913
Entered Medline: 19990902

AB **Spider** bites due to Loxosceles intermedia are currently a major public health problem in South Brazil. About 3000 cases are reported annually. Specific **treatment** for **spider** bites is provided by the polyvalent anti-arachnidic antiserum produced by Butantan Institute, Sao Paulo, Brazil by **immunizing** horses with mixtures of **venoms** from Tityus serrulatus and T. bahiensis scorpions, as well as Phoneutria nigriventer and L. gaucho **spiders**. Due to the large amounts of the anti-arachnidic **antivenom** required and since L. intermedia **venom** has some biochemical and pharmacological variations, we have produced a specific anti-L. intermedia **antivenom**. This study shows that horses **immunized** with crude L. intermedia **venom** produced IgG antibodies that neutralized the dermonecrotic and lethal activities of the **venom** . The neutralizing potency of the anti-loxoscelic **antivenom** was compared with that of the anti-arachnidic **antivenom**. Our results indicate that both **antivenoms** were effective in terms of neutralization. However, the anti-loxoscelic **antivenom** was more efficient than the anti-arachnidic.

L27 ANSWER 10 OF 36 MEDLINE
ACCESSION NUMBER: 1998214214 MEDLINE
DOCUMENT NUMBER: 98214214 PubMed ID: 9553598
TITLE: When to worry about spider bites. Inaccurate diagnosis can have serious, even fatal, consequences.
AUTHOR: Koh W L
CORPORATE SOURCE: Kaiser-Fontana Medical Center, California 92335, USA..
wui.l.koh@kp.org
SOURCE: POSTGRADUATE MEDICINE, (1998 Apr) 103 (4) 235-6, 243-4, 249-50. Ref: 9
Journal code: PFK; 0401147. ISSN: 0032-5481.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199805
ENTRY DATE: Entered STN: 19980514
Last Updated on STN: 19980514
Entered Medline: 19980506

AB Almost all species of **spiders** are capable of biting people, but the bites of only a few are medically significant. Physicians need to be able to recognize the clinical signs and symptoms of common **venomous spider** bites and administer appropriate **therapy**. This may be difficult, since the offending **spider** is rarely seen or recovered for identification. Knowledge of life cycles, habits, and toxicity of **venomous spiders** enables physicians to provide more comprehensive medical care of bite victims. It is hoped that study of **immunologic** mechanisms and inflammation mediators will lead to the development of new **treatments**.

=> d ibib abs kwic 11-20
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L27 ANSWER 11 OF 36 MEDLINE
ACCESSION NUMBER: 87324352 MEDLINE
DOCUMENT NUMBER: 87324352 PubMed ID: 2888425
TITLE: Jellyfish envenomation syndromes updated.
AUTHOR: Burnett J W; Calton G J
SOURCE: ANNALS OF EMERGENCY MEDICINE, (1987 Sep) 16 (9) 1000-5.
Ref: 43
Journal code: 4Z7; 8002646. ISSN: 0196-0644.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English

FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 198710
ENTRY DATE: Entered STN: 19900305
Last Updated on STN: 19950206
Entered Medline: 19871001

AB **Jellyfish venoms** are mixtures of toxic and/or antigenic polypeptides and enzymes pathogenic to human beings. As newer **therapeutic** agents become available to **treat** the various reactions to stings caused by these animals, an accurate diagnosis of the type of reaction the patient experiences and of the offending species will be necessary. Fatal reactions may be caused either by anaphylaxis or by the action of toxins in the **venom** on the heart, respiratory center, or kidneys. Cutaneous eruptions after **envenomation** may be local, generalized, exaggerated, recurrent, delayed, persistent, or occur at sites distant from the primary sting. Fat atrophy, pigmentary changes, vasospasm, and contractures with gangrene can occur after **jellyfish** stings. Identification of the **envenoming** animal can be made by actual visualization, examination for nematocysts on skin scraping, or serologically. It may also be predicted based on knowledge of location, time, and environmental circumstances of the encounter. First-aid measures designed to prevent additional nematocyst rupture are species-specific. Anaphylaxis should be prevented by the appropriate lifesaving measures. Other syndromes, caused by the toxins of the **venom** or mediated by humoral or cellular **immune** mechanisms, should be **treated** specifically.

L27 ANSWER 12 OF 36 MEDLINE
ACCESSION NUMBER: 1999180197 MEDLINE
DOCUMENT NUMBER: 99180197 PubMed ID: 10082160
TITLE: Oligosaccharide residues of Loxosceles intermedia (brown spider) venom proteins: dependence on glycosylation for dermonecrotic activity.
AUTHOR: Veiga S S; Gremski W; dos Santos V L; Feitosa L; Mangili O C; Nader H B; Dietrich C P; Brentani R R
CORPORATE SOURCE: Department of Cell Biology, Federal University of Parana, Jardim das Americas, Curitiba, Brazil.
SOURCE: TOXICON, (1999 Apr) 37 (4) 587-607.
Journal code: VWT; 1307333. ISSN: 0041-0101.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199906
ENTRY DATE: Entered STN: 19990628
Last Updated on STN: 19990628
Entered Medline: 19990614

AB Loxosceles spp. (brown **spider**) **envenomation** has been reported to provoke dermonecrosis and haemorrhage at the bite site (a hallmark of accidents) and, to a lesser extent, thrombocytopenia, hemolysis and disseminated intravascular coagulation in some cases. Using lectin-**immunolabeling**, lectin-affinity chromatography, glycosidase and proteinase K **treatments** we were able to identify several **venom** N-glycosylated proteins with high-mannose oligosaccharide structures, complex-type glycoconjugates such as fucosylated glycans, but no galactose or sialic acid residues as complex sugars or glycosaminoglycan residues. Working with enzymatically or chemically deglycosylated **venom** we found that platelet aggregation (thrombocytopenic activity) as well as the fibronectinolytic and fibrinogenolytic (haemorrhagic) effects of the **venom** were sugar-independent when compared to glycosylated **venom**. Nevertheless, zymograph analysis in co-polymerized gelatin gels showed that enzymatic N-deglycosylation of loxolysin-B, a high-mannose 32-35 kDa glycoprotein of the **venom** with gelatinolytic metalloproteinase activity, caused a reduction of approximately 2 kDa in its molecular weight and a reduction of the gelatinolytic effect to a residual activity of 28% when compared to the glycosylated molecule, indicating a post-translational glycosylation-dependent gelatinolytic effect. Analysis of the dermonecrotic effect of the chemically or enzymatically N-deglycosylated **venom** detected only residual activity when compared with the glycosylated control. Thus, the present report suggests that oligosaccharide moieties play a role in the destructive effects of brown **spider venom** and opens the possibility for a carbohydrate-based **therapy**.

L27 ANSWER 13 OF 36 MEDLINE
ACCESSION NUMBER: 82029419 MEDLINE
DOCUMENT NUMBER: 82029419 PubMed ID: 7287056
TITLE: Alternate complement pathway activation by recluse spider venom.
AUTHOR: Kurpiewski G; Campbell B J; Forrester L J; Barrett J T
SOURCE: INTERNATIONAL JOURNAL OF TISSUE REACTIONS, (1981 Mar) 3 (1) 39-45.
Journal code: GTG; 8302116. ISSN: 0250-0868.
PUB. COUNTRY: Switzerland
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198112
ENTRY DATE: Entered STN: 19900316
Last Updated on STN: 19900316
Entered Medline: 19811219

AB **Venom** from the poisonous brown recluse **spider** (Loxosceles reclusa) catalyses the lysis of dithiothreitol-**treated** human erythrocytes when incubated with serum complement but not in heat inactivated serum, a characteristic of complement system activation via the alternate pathway. This activity of the **venom** was shown to reside in a Sephadex G-75 fraction of the **venom** which also contains the dermonecrotoxin. Isoelectric focusing of this fraction identified the complement inactivating molecules(s) in the region near pH=6. Analysis of complement after interaction with **venom** indicated a loss of haemolytic C3. **Immunoelectrophoretic** development of **venom**-complement mixtures with anti C3 proactivator revealed the appearance of the C3 activator. These data indicate that recluse **spider venom** activates the alternate complement pathway.

L27 ANSWER 14 OF 36 MEDLINE
ACCESSION NUMBER: 2000158515 MEDLINE
DOCUMENT NUMBER: 20158515 PubMed ID: 10695968
TITLE: Identification of high molecular weight serine-proteases in Loxosceles intermedia (brown spider) venom.
AUTHOR: Veiga S S; da Silveira R B; Dreyfus J L; Haoach J; Pereira A M; Mangili O C; Gremski W
CORPORATE SOURCE: Department of Cell Biology, Federal University of Parana, Curitiba, Brazil.. veigass@bio.ufpr.br
SOURCE: TOXICON, (2000 Jun) 38 (6) 825-39.
Journal code: VWT; 1307333. ISSN: 0041-0101.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200004
ENTRY DATE: Entered STN: 20000421
Last Updated on STN: 20000421
Entered Medline: 20000412

AB High molecular weight serine-proteases have been identified in Loxosceles intermedia (brown **spider**) **venom**. The mechanism by which Loxosceles spp **venoms** cause dermonecrotic injury (a hallmark of loxoscelism) is currently under investigation, but it seems to be molecularly complex and in some instance proteases might be expected to play a role in this skin lesion. In the present investigation, when we submitted L. intermedia **venom** to linear gradient 3-20% SDS-PAGE stained by a monochromatic silver method we detected a heterogeneous protein profile in molecular weight, ranging from 850- to 5-kDa. In an attempt to detect zymogen molecules of proteolytic enzymes, **venom** aliquots were **treated** with several exogenous proteases. Among them, trypsin activated two gelatinolytic molecules of 85- and 95-kDa in the **venom**. In experiments of hydrolysis inactivation using different protease inhibitors for four major class of proteases, we detected that only serine-type protease inhibitors were able to inactivate the 85- and 95-kDa enzymes in the **venom**. An examination of the 85- and 95-kDa gelatinolytic activities as a function of pH showed that these proteases had no apparent activities at pH below 5.0 and higher than 9.0 and displayed little activity at pH 6.0. with the optimal pH for their activities ranging from 7.0 to 8.0. Evaluation of the functional specificities of the 85- and 95-kDa **venom** proteases showed that

these proteases efficiently degrade gelatin (denatured collagen) but have no proteolytic activity on hemoglobin, **immunoglobulin**, albumin, librinogen or laminin, suggesting specificity of their proteolytic actions. We describe here two serine-proteases activities in L. intermedia **venom** probably involved in the harmful effects of the **venom**.

L27 ANSWER 15 OF 36 MEDLINE
ACCESSION NUMBER: 94088356 MEDLINE
DOCUMENT NUMBER: 94088356 PubMed ID: 8264466
TITLE: Venomous bites and stings in the tropical world.
AUTHOR: Warrell D A
CORPORATE SOURCE: University of Oxford, Nuffield Department of Clinical Medicine, John Radcliffe Hospital, Headington, UK.
SOURCE: MEDICAL JOURNAL OF AUSTRALIA, (1993 Dec 6-20) 159 (11-12) 773-9. Ref: 30
Journal code: M26; 0400714. ISSN: 0025-729X.
PUB. COUNTRY: Australia
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199401
ENTRY DATE: Entered STN: 19940209
Last Updated on STN: 19940209
Entered Medline: 19940125

AB Snakes of the families Viperidae and Elapidae are responsible for the high incidence of morbidity and mortality after snake bites in countries of West Africa, the Indian subcontinent, South-East Asia, New Guinea and Latin America. **Envenoming** can cause local effects, notably tissue necrosis; and systemic effects, including paralysis, haemostatic disturbances, shock, increased capillary permeability, myocardial damage, rhabdomyolysis and acute renal failure. Specific **hyperimmune** serum (**antivenom**) is the mainstay of medical **treatment** for severe **envenoming**. Ancillary **treatments** such as assisted ventilation, repletion of circulating volume, renal dialysis and surgical debridement of necrotic tissues are needed in some cases. Scorpion stings are a common medical problem in middle and southern America, North Africa and the Middle East. Vasodilator drugs are important to counter the effects of massive catecholamine release. Bites by **spiders** and stings by hymenoptera and marine animals are responsible for deaths and morbidity in some tropical countries.

L27 ANSWER 16 OF 36 MEDLINE
ACCESSION NUMBER: 86140993 MEDLINE
DOCUMENT NUMBER: 86140993 PubMed ID: 2869072
TITLE: Jellyfish envenomation syndromes.
AUTHOR: Burnett J W; Calton G J; Burnett H W
SOURCE: JOURNAL OF THE AMERICAN ACADEMY OF DERMATOLOGY, (1986 Jan) 14 (1) 100-6. Ref: 33
Journal code: HVG; 7907132. ISSN: 0190-9622.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198604
ENTRY DATE: Entered STN: 19900321
Last Updated on STN: 19950206
Entered Medline: 19860407

AB **Jellyfish venoms** are complex mixtures of polypeptides and enzymes pathogenic to man by means of their toxic or antigenic properties. With newer technology, more **therapeutic** agents will become available to **treat** the various **envenomation** syndromes caused by these animals. It will therefore be necessary to make an accurate diagnosis of the type of reaction the patient experiences, as well as to identify the offending species. Fatal reactions can be caused by hypersensitivity or induced by various toxins on the heart, respiratory center, or kidney. Cutaneous eruptions may be local or generalized, have exaggerated local edema, become recurrent, be delayed and persistent, or occur at sites distant from the primary sting. Fat atrophy, pigmentary changes, and contractures with gangrene can also appear. Identification of

the responsible coelenterate can be made directly by actual visualization or indirectly by the knowledge of location, time, and environmental circumstances of the stinging. First-aid measures designed to prevent additional nematocyst rupture appear to be species-specific. Anaphylaxis should be counteracted by the lifesaving measures required. Other syndromes, either caused by toxic effects of the **venom** or mediated by humoral or cellular **immune** mechanisms, should be **treated** by means designed to interfere with their pathogenesis.

L27 ANSWER 17 OF 36 MEDLINE
ACCESSION NUMBER: 85018202 MEDLINE
DOCUMENT NUMBER: 85018202 PubMed ID: 6385462
TITLE: Effects of various treatments of bovine complement on its lytic efficacy measured by two different tests.
AUTHOR: Nielsen K; Rosenbaum B; Ballinger R; Stiller J
SOURCE: VETERINARY IMMUNOLOGY AND IMMUNOPATHOLOGY, (1984 Jul) 6 (3-4) 273-83.
Journal code: XCB; 8002006. ISSN: 0165-2427.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198411
ENTRY DATE: Entered STN: 19900320
Last Updated on STN: 19900320
Entered Medline: 19841105

AB Bovine complement was **treated** with various agents known to activate or inactivate one or more of the cascade components. The **treated** complement was then assessed for remaining hemolytic activity by a tube titration test and a radial hemolysis method. Divalent cation chelators (EDTA and EGTA); **immune** complexes prepared with serum and IgM, IgG1, IgG2, and IgA isotypes; smooth and rough lipopolysaccharides and lipid A; hydrazine; zymosan; cobra **venom** factor and brown recluse **spider venom** caused depletion of complement as determined in the tube titration test. **Immune** complexes (prepared with serum); hydrazine; cobra **venom** factor; EDTA and smooth lipopolysaccharide caused loss of hemolytic activity in the radial hemolysis test. This evidence suggests that the radial hemolysis test assessed complement consumed by the alternate pathway, while the tube titration method measured classical pathway consumption.

L27 ANSWER 18 OF 36 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1996:751503 CAPLUS
DOCUMENT NUMBER: 126:17801
TITLE: Variable domains of the two-chain immunoglobulins of camelids and their therapeutic and veterinary use
INVENTOR(S): Hamers, Raymond; Muyldersmans, Serge
PATENT ASSIGNEE(S): Vrije Universiteit Brussel, Belg.
SOURCE: Eur. Pat. Appl., 38 pp
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 739981	A1	19961030	EP 1995-400932	19950425
R: GB				
WO 9634103	A1	19961031	WO 1996-EP1725	19960425
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN				
AU 9656478	A1	19961118	AU 1996-56478	19960425
EP 822985	A1	19980211	EP 1996-913525	19960425
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 11503918	T2	19990406	JP 1996-532171	19960425

PRIORITY APPLN. INFO.: EP 1995-400932 19950425
WO 1996-EP1725 19960425

AB Variable domain regions derived from the heavy chains of the two-chain Ig heavy chains of camelids are described for therapeutic use. Selection of coding sequences for variable domains binding specific antigens using phage display libraries is described. PCR primers for use in the cloning of these sequences are described. The selection of antibodies to tetanus toxoid by panning is demonstrated.

IT Bee
Coral
Crotalidae
Jellyfish
Scorpion
Sea anemone
Snake
Spider
Viperidae
Wasp
(selection of dromedary antibodies to toxin or **venom** of; variable domains of two-chain **Igs** of camelids and their **therapeutic** and veterinary use)

L27 ANSWER 19 OF 36 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2001:416998 CAPLUS
DOCUMENT NUMBER: 135:32739
TITLE: Immunogen, antivenom and vaccine against the venom of the black widow spider
INVENTOR(S): Gurrola Briones, Georgina; Alagon Cano, Alejandro; Possani Postay, Lourival Domingos; Grishin, Eugene Vasilevich; Lipkin, Alexei Valerevich; Volynski, Kirill Evgenevich
PATENT ASSIGNEE(S): Universidad Nacional Autonoma de Mexico, Mex.; Shemyakin and Ovchinnikov Institute of Bioorganic Chemistry
SOURCE: PCT Int. Appl., 59 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Spanish
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001040290	A1	20010607	WO 2000-MX48	20001128

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: MX 1999-11191 A 19991203
AB The invention relates to a recombinant polypeptide that comprises the N-terminal region of .alpha.-Latrotoxin, is capable of generating an immune response in mammals, and efficiently and fully neutralizes the venom of the black widow spider. The invention also relates to the cDNA coding for said polypeptide, the vector for the expression thereof, the bacterial cells transformed with said vector, and a method for producing the polypeptide by means of culture of said cells. The invention further relates to the use of said recombinant polypeptide as a vaccine against the venom of the black widow spider and to pharmaceutically prepns. of said vaccine. The invention addnl. relates to the use of said recombinant polypeptide as **immunogen** for generating **antivenom** serum for the black widow **spider**, obtaining serotherapeutic agents by serum purifn. and Fab **therapeutic** agents by enzymic hydrolysis of the antibodies of the serum. The invention also relates to an immunogen matrix that is useful in the sepn. and purifn. of antibodies and antibody fragments against the venom of the black widow spider.
REFERENCE COUNT: 3
REFERENCE(S): (1) British Tech Group; WO 9529235 A 1995 CAPLUS
(2) Grinshin, E; TOXICON 1998, V36(11), P1693
(3) Kiyatkin, N; FEBS LETTERS 1990, V270(1,2), P127

L27 ANSWER 20 OF 36 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1995:502715 BIOSIS
DOCUMENT NUMBER: PREV199598526265
TITLE: Antibodies as therapeutic agents: The antivenoms.
AUTHOR(S): Dart, Richard C.
CORPORATE SOURCE: Rocky Mountain Poison Center, 645 Bannock St., Denver, CO 80204 USA
SOURCE: Journal of Natural Toxins, (1995) Vol. 4, No. 2, pp. 155-163.
ISSN: 1058-8108.
DOCUMENT TYPE: Article
LANGUAGE: English
AB All **therapeutic** agents must be proven effective and safe. Monoclonal antibody (MAb) for **treatment** of septic shock is safe, but not effective. Polyclonal Fab (e.g., digoxin Fab), however, is effective as well as safe. There are several differences between the two: MAb binds only one epitope, while polyclonal antibody binds many epitopes on the same molecule. MAb is an IgG, while the other is Fab. An IgG molecule is composed of three parts, two Fab and one Fc. The Fab is the neutralizing portion. Digoxin Fab is produced by **immunizing** sheep with digoxin and adjuvant, harvesting of the blood, and then isolating the IgG. The IgG is then digested with papain to Fab and Fe. Finally, the Fc is removed and the remaining product lyophilized. Antivenins are a natural choice for polyclonal Fab application. The current rattlesnake antivenin is made by **immunizing** horses with **venom**, harvesting the blood, partially purifying the serum (to concentrate the IgG), and then administering the serum to patients. Because it contains IgG and other proteins, it may cause allergic reactions, including anaphylaxis and serum sickness. Clinical trials of the new antivenin, Polyvalent Crotalidae Antivenin (Ovine Fab) are underway in the United States. Preliminary research indicates efficacy and minimal adverse reactions. In Sweden, Fab antivenin to the snake Vipera berus has already been proven effective and safe. Other promising applications of polyclonal Fab include the tricyclic antidepressants and the **venoms** of the **spiders** Latrodectus mactans and Loxosceles reclusa.

=> d ibib abs kwic 21-36
YOU HAVE REQUESTED DATA FROM FILE 'MEDLINE, CAPLUS, BIOSIS, USPATFULL' - CONTINUE? (Y)/N:y

L27 ANSWER 21 OF 36 MEDLINE
ACCESSION NUMBER: 94143898 MEDLINE
DOCUMENT NUMBER: 94143898 PubMed ID: 7906057
TITLE: Immunity to jellyfish venoms: suppression of venom-induced immune responses in ultraviolet B-irradiated mice.
AUTHOR: Miura S; Burnett J W; Aurelian L
CORPORATE SOURCE: Department of Dermatology, University of Maryland School of Medicine, Baltimore 21201.
CONTRACT NUMBER: AI 22192 (NIAID)
SOURCE: TOXICON, (1993 Nov) 31 (11) 1415-22.
Journal code: VWT; 1307333. ISSN: 0041-0101.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199403
ENTRY DATE: Entered STN: 19940330
Last Updated on STN: 19950206
Entered Medline: 19940317
AB Lymph node and spleen cells from mice **immunized** with sea nettle (Chrysaora quinquecirrha) **venom** exhibited a proliferative response after exposure to the homologous antigen or that of a related **jellyfish**, Physalia (Portuguese man-o'-war). Native **venom** was a more effective stimulant than heated, non-lethal **venom**. Ultraviolet light **treatments** administered to the skin either before or after **venom** sensitization suppressed the proliferative response of these internal **immune** cells.

L27 ANSWER 22 OF 36 MEDLINE
ACCESSION NUMBER: 88116573 MEDLINE
DOCUMENT NUMBER: 88116573 PubMed ID: 2892880

TITLE: Erythema nodosum following a jellyfish sting.
AUTHOR: Auerbach P S; Hays J T
CORPORATE SOURCE: Vanderbilt University Hospital, Nashville, Tennessee.
SOURCE: JOURNAL OF EMERGENCY MEDICINE, (1987 Nov-Dec) 5 (6) 487-91.
Journal code: IBO; 8412174. ISSN: 0736-4679.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198803
ENTRY DATE: Entered STN: 19900308
Last Updated on STN: 19950206
Entered Medline: 19880318

AB At least 100 of the approximately 9,000 species of coelenterates are dangerous to humans. The most common syndrome following an **envenomation** is an immediate intense dermatitis, with characteristic skin discoloration, local pain, and systemic symptoms. In this case report, we describe a case of erythema nodosum with articular manifestations following **envenomation** with an unknown **jellyfish**. Serological testing of the victim revealed marked elevation of **immunoglobulins** G and M directed against Physalia physalis, the Portuguese man-of-war. The patient's condition did not respond to conventional topical **therapy** for coelenterate **envenomation**, but was successfully managed with systemic corticosteroid **therapy**. This case demonstrates that the emergency physician should consider a delayed reaction to a marine **envenomation** in any victim who presents with an acute dermatological disease following immersion in marine coastal waters.

L27 ANSWER 23 OF 36 MEDLINE
ACCESSION NUMBER: 82200189 MEDLINE
DOCUMENT NUMBER: 82200189 PubMed ID: 6123162
TITLE: Some clinical and epidemiological problems of venom poisoning today.
AUTHOR: Maretic Z
SOURCE: TOXICON, (1982) 20 (1) 345-8.
Journal code: VWT; 1307333. ISSN: 0041-0101.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198207
ENTRY DATE: Entered STN: 19900317
Last Updated on STN: 19950206
Entered Medline: 19820708

AB Poisonings caused by bites and stings of **venomous** animals have not lost their importance from most ancient times until today. Rather, one could say that they in some respects have become even more important due to some moments as: the interesting results of biochemical, pharmacological and **immunological** researches of their **venoms**, so as possibilities of their use in **treatment** and in preparation of drugs; the importation of **venomous** animals in loads of goods from countries with warm climate into countries where they normally would not be found; the increasing number of fanciers who keep in their terraria often very dangerous animals; the interest of most armies of the world for **venomous** animals and poisonings due to them. However, the author stressed the increasing importance of **venomous** stings and bites from the point of view of modern tourism. The epidemiological and clinical features of poisoning by some animals in tourists are described: so for instance the consequences of bites and stings of **spiders**, gad flies, scolopendras, scorpions, coelenterates and fishes.

L27 ANSWER 24 OF 36 MEDLINE
ACCESSION NUMBER: 92023281 MEDLINE
DOCUMENT NUMBER: 92023281 PubMed ID: 1926163
TITLE: Protection of monkeys against the lethal effects of male funnel-web spider (Atrax robustus) venom by immunization with a toxoid.
AUTHOR: Sheumack D D; Phillips C A; Mylecharane E J; Spence I; Claassens R; Brown M R; Comis A; Howden M E
CORPORATE SOURCE: School of Chemistry, Macquarie University, North Ryde, N.S.W., Australia.
SOURCE: TOXICON, (1991) 29 (6) 603-11.

Journal code: VWT; 1307333. ISSN: 0041-0101.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199111
ENTRY DATE: Entered STN: 19920124
Last Updated on STN: 19920124
Entered Medline: 19911121

AB A stable toxoid was prepared from robustoxin (the lethal polypeptide neurotoxin in the **venom** of the male funnel-web **spider**, Atrax robustus) by polymerization with glutaraldehyde. This material was non-toxic in new-born mice. Administration of the toxoid to three Macaca fascicularis monkeys (50-80 micrograms/kg s.c. at 14-day intervals for 8-12 weeks) produced no toxic effects; anti-robustoxin antibodies were detected in serum samples by **immunodiffusion** tests within 13-27 days. In vivo evidence of successful protection with the toxoid was obtained by challenging the monkeys with male A. robustus **venom** (50 micrograms/kg i.v.) under anaesthesia with pentobarbitone (one monkey), or with ketamine, halothane and nitrous oxide, 1-26 weeks after the last injection of the toxoid. Only minor respiratory, cardiovascular and skeletal motor disturbances were produced, and all monkeys recovered fully and uneventfully. Challenge with the same dose of **venom** in non-**immunized** or robustoxin N-terminal decapeptide ovalbumin conjugate-**treated** monkeys resulted in typical lethal neurotoxic effects, culminating in severe hypotension or death from circulatory and respiratory failure within 280 min.

L27 ANSWER 25 OF 36 MEDLINE
ACCESSION NUMBER: 91275457 MEDLINE
DOCUMENT NUMBER: 91275457 PubMed ID: 1675965
TITLE: An endogenous antitoxin to the lethal venom of the funnel web spider, Atrax robustus, in rabbit sera.
AUTHOR: Sheumack D D; Comis A; Claassens R; Mylecharane E J; Spence I; Howden M E
CORPORATE SOURCE: School of Chemistry, Macquarie University, North Ryde, NSW.
SOURCE: COMPARATIVE BIOCHEMISTRY AND PHYSIOLOGY. C: COMPARATIVE PHARMACOLOGY AND TOXICOLOGY, (1991) 99 (1-2) 157-61.
Journal code: DNX; 8310013. ISSN: 0742-8413.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199108
ENTRY DATE: Entered STN: 19910818
Last Updated on STN: 19950206
Entered Medline: 19910801

AB 1. An endogenous antitoxin fraction was isolated from non-**immune** rabbit sera by affinity chromatography with robustoxin bound to the solid support. 2. Robustoxin is the sole lethal toxin in the **venom** of the male funnel web **spider**, Atrax robustus. 3. The fraction was found to contain IgG and IgM **immunoglobulins**. 4. This fraction prevented or reversed the lethal actions of the crude **venom** in newborn mice, in mouse phrenic nerve-hemidiaphragm preparations, and in anaesthetized monkeys. 5. The antitoxin fraction is of potential value in the **therapy** of human **envenomation** by A. robustus.

L27 ANSWER 26 OF 36 USPATFULL
ACCESSION NUMBER: 84:52632 USPATFULL
TITLE: Blood purification method
INVENTOR(S): Tanihara, Masao, Kurashiki, Japan
Nakashima, Toshihide, Kurashiki, Japan
Takakura, Koichi, Okayama, Japan
PATENT ASSIGNEE(S): Kuraray Co., Ltd., Kurashiki, Japan (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 4472303		19840918
APPLICATION INFO.:	US 1983-524931		19830822 (6)
RELATED APPLN. INFO.:	Division of Ser. No. US 1982-395975, filed on 7 Jul 1982, now patented, Pat. No. US 4420395		

	NUMBER	DATE
PRIORITY INFORMATION:	JP 1981-108670	19810710

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Therkorn, Ernest G.
LEGAL REPRESENTATIVE: Kramer, Barry
NUMBER OF CLAIMS: 9
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 4 Drawing Figure(s); 2 Drawing Page(s)
LINE COUNT: 458

AB Treatment of the blood by means of a blood purification device comprising packed, substantially spherical, smooth-surfaced, porous granules having at least 0.1 .mu.mole/m.sup.2 of the silanol group on the surface thereof, a blood inlet and a blood outlet scarcely causes decrease in leukocyte or platelet count or blood cell damage and can remove proteins from the blood by adsorption without high pressure loss.

DETD . . . the protein species adsorbed. For instance, for adsorption of proteins having a molecular weight of 500 to 20,000, such as **immune** soluble factors (e.g. cancer cell-derived **immunosuppressive** factor:IRA (**immuno**-regulatory .alpha.-globulin), T-lymphocyte-derived **immune** soluble factors: TCGF (T cell growth factor), GSF (growth soluble factor), SSF (suppressor soluble factor), TRF (T cell replacing factor). . . and CIF (competence-inducing factor), and macrophage-derived factors:TDF (thymocyte-differentiation factor) and interleukin I), lysozyme, cytochrome C and toxic proteins secreted by **venomous** snake, scorpion, nocuous sea urchin, **venomous spider**, frog, wasp, bee and so on, the granules preferably have a mean pore diameter within the range of 20-150 angstroms.. . . such as amino respectively onto the surface. For proteins with a molecular weight of 20,000-200,000, such as .gamma.-globulin, albumin and **immunosuppressive** factors, including .alpha..sub.1 -antitrypsin (.alpha..sub.1 AT), C-reactive protein (CRP), .alpha..sub.1 -acid glycoprotein (AAG), **immunosuppressive** acid protein (IAP) and .alpha.-fetoprotein (AFP), the granules preferably have a mean pore diameter within the range of 150-1,000 angstroms. .gamma.-Globulin is a group of proteins with a molecular weight of about 160,000. Among them, **immunoglobulin** G is the main causative factor in **autoimmune** diseases. Removal of such causative factor from the blood can contribute to the **treatment** of the relevant diseases. For adsorption of .gamma.-globulin, the use of porous granules having a mean pore diameter of 350-900. . . pore diameter within the range of 900-1,600 angstroms is preferable and, for proteins having a molecular weight of 200,000-1,000,000, including **immune** complexes, fibrinogen, microfibrin and complements, the mean pore diameter is preferably within the range of 1,000-2,500 anstroms.

L27 ANSWER 27 OF 36 USPATFULL
ACCESSION NUMBER: 83:58680 USPATFULL
TITLE: Blood purification device
INVENTOR(S): Tanihara, Masao, Kurashiki, Japan
Nakashima, Toshihide, Kurashiki, Japan
Takakura, Koichi, Okayama, Japan
PATENT ASSIGNEE(S): Kuraray Co., Ltd., Kurashiki, Japan (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 4420395		19831213
APPLICATION INFO.:	US 1982-395975		19820707 (6)

	NUMBER	DATE
PRIORITY INFORMATION:	JP 1981-108670	19810710

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Therkorn, Ernest G.
LEGAL REPRESENTATIVE: Kramer, Barry
NUMBER OF CLAIMS: 13
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 4 Drawing Figure(s); 2 Drawing Page(s)

LINE COUNT: 465

AB Treatment of the blood by means of a blood purification device comprising packed, substantially spherical, smooth-surfaced, porous granules having at least 0.1 .mu.mole/m.sup.2 of the silanol group on the surface thereof, a blood inlet and a blood outlet scarcely causes decrease in leukocyte or platelet count or blood cell damage and can remove proteins from the blood by adsorption without high pressure loss.

DETD . . . the protein species adsorbed. For instance, for adsorption of proteins having a molecular weight of 500 to 20,000 such as **immune** soluble factors (e.g. cancer cell-derived **immunosuppressive** factor: IRA (**immuno**-regulatory .alpha.-globulin), T-lymphocyte-derived **immune** soluble factors: TCGF (T cell growth factor), GSF (growth soluble factor), SSF (suppressor soluble factor), TRF (T cell replacing factor). . . . CIF (competence-inducing factor), and macrophage-derived factors: TDF (thymocyte-differentiation factor) and interleukin I), lysozyme, cytochrome C and toxic proteins secreted by **venomous** snake, scorpion, nocuous sea urchin, **venomous spider**, frog, wasp, bee and so on, the granules preferably have a mean pore diameter within the range of 20-150 angstroms.. . . such as amino respectively onto the surface. For proteins with a molecular weight of 20,000-200,000, such as .gamma.-globulin, albumin and **immunosuppressive** factors, including .alpha..sub.1 -antitrypsin (.alpha..sub.1 AT), C-reactive protein (CRP), .alpha..sub.1 -acid glycoprotein (AAG), **immunosuppressive** acid protein (IAP) and .alpha.-fetoprotein (AFP), the granules preferably have a mean pore diameter within the range of 150-1,000 angstroms. .gamma.-Globulin is a group of proteins with a molecular weight of about 160,000. Among them, **immunoglobulin** G is the main causative factor in **autoimmune** diseases. Removal of such causative factor from the blood can contribute to the **treatment** of the relevant diseases. For adsorption of .gamma.-globulin, the use of porous granules having a mean pore diameter of 350-900. . . pore diameter within the range of 900-1,600 angstroms is preferable and, for proteins having a molecular weight of 200,000-1,000,000, including **immune** complexes, fibrinogen, microfibrin and complements, the mean pore diameter is preferably within the range of 1,000-2,500 anstroms.

L27 ANSWER 28 OF 36 MEDLINE

ACCESSION NUMBER: 91143374 MEDLINE
DOCUMENT NUMBER: 91143374 PubMed ID: 2288242
TITLE: Motor nerve terminal restoration after focal destruction in young and old mice.
AUTHOR: Robbins N; Kuchynski M; Polak J; Grasso A
CORPORATE SOURCE: Center for Neurosciences, Case Western Reserve University School of Medicine, Cleveland, Ohio 44106.
CONTRACT NUMBER: AG06641 (NIA)
AG08886 (NIA)
SOURCE: INTERNATIONAL JOURNAL OF DEVELOPMENTAL NEUROSCIENCE, (1990) 8 (6) 667-78.
Journal code: 126; 8401784. ISSN: 0736-5748.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199103
ENTRY DATE: Entered STN: 19910412
Last Updated on STN: 19910412
Entered Medline: 19910325

AB Regeneration of soleus motor nerve terminals after focal destruction by black widow **spider venom** (BWSV) or its active factor alpha-latrotoxin (LTx) was compared in young and old CBF-1 mice. The object was to determine whether previously reported delayed regeneration after nerve injury in old rodents was due to altered removal of debris, or delay or aberrancy in structural or functional restoration of the neuromuscular junction. In addition, the use of a new fluorescent technique permitted for the first time quantitation of the accuracy of early nerve terminal regeneration in mammalian muscle. **Immunohistochemical** and electron micrographic studies showed no age difference in destruction of terminals and removal of debris 2 days after toxin application. The indirect twitch and structural reinnervation (measured with flourescent techniques) returned to an equal extent in

young and old mice beginning at 3 days after LTx **treatment**. BWSV (as opposed to LTx) delayed regeneration 1 day in young but not in old mice. On the first day of reinnervation, there was perisynaptic outgrowth in both young and old mice, although in the latter, there was a higher incidence of aberrant outgrowth. The relation between return of twitch strength and recovery of nerve terminal area (measured in teased zinc iodide-stained preparations) showed no age dependency. We conclude that factors cited to explain altered reactive sprouting in the aging CNS do not apply to regeneration of peripheral motor nerve terminals. However, it is possible that the aberrant regrowth observed at the neuromuscular junction in old mice will pertain to the aging CNS. Altered axonal rather than nerve terminal regeneration is the likely source of delayed peripheral nerve regeneration in old animals.

L27 ANSWER 29 OF 36 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1992:606831 CAPLUS
DOCUMENT NUMBER: 117:206831
TITLE: IgG antibodies to Loxosceles sp. spider venom in human envenoming
AUTHOR(S): Barbaro, K. C.; Cardoso, J. L. C.; Eickstedt, V. R. D.; Mota, I.
CORPORATE SOURCE: Cent. Pesqui. Formacao Imunol. Prof. Otto G. Bier, Inst. Butantan, Sao Paulo, 05504, Brazil
SOURCE: Toxicon (1992), 30(9), 1117-21
CODEN: TOXIA6; ISSN: 0041-0101
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The presence and specificity of IgG antibodies produced by patients with loxoscelism were studied. The loxoscelism diagnosis was supported mainly by clin. parameters. A search for IgG antibodies to L. gaucho venom in patients with loxoscelism submitted to serum therapy showed antibodies in 4 out of 20 patients. The IgG antibodies were detected as early as 9 days and as late as 120 days after bite. The highest IgG antibody titer was 1:640 and the lowest was 1:80. Immunoblotting tests showed that human anti-L. gaucho IgG antibodies recognize preferentially the components responsible for the dermonecrotic and lethal activities of the venom. A comparison of the clin. picture, the level of serum IgG antibodies, and the dose of antivenom administered suggest that there is no relationship between these parameters.

IT **Immunoglobulins**
RL: BIOL (Biological study)
(G, to Loxosceles **spider venom**, in humans, **antivenom treatment** in relation to)

L27 ANSWER 30 OF 36 MEDLINE
ACCESSION NUMBER: 2001693948 IN-PROCESS
DOCUMENT NUMBER: 21605843 PubMed ID: 11738237
TITLE: Apoptosis induced by box jellyfish (Chiropsalmus Quadrigatus) toxin in glioma and vascular endothelial cell lines.
AUTHOR: Sun Lian Kun; Yoshii Yoshihiko; Hyodo Akio; Tsurushima Hideo; Saito Atsushi; Harakuni Tsuyoshi; Li Ya Ping; Nozaki Masatoshi; Morine Nobuya
CORPORATE SOURCE: Department of Neurosurgery, Faculty of Medicine, University of the Ryukyus, Nishihara Uehara 207, 903-0215, Okinawa, Japan.
SOURCE: TOXICON, (2002 Apr) 40 (4) 441-6.
Journal code: VWT; 1307333. ISSN: 0041-0101.
PUB. COUNTRY: England: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE: Entered STN: 20011217
Last Updated on STN: 20011217

AB This study was made to investigate whether Chiropsalmus Quadrigatus toxins (CqTX), which isolated from box **jellyfish** C. Quadrigatus **venom**, could induce apoptosis in human U251 and rat C6 malignant glioma cells and transformed vascular endothelial ECV 304 cell lines. Cell viability was estimated by MTT assay. Apoptosis was evaluated using TdT (terminal deoxynucleotidyl transferase)-mediated dUTP nick-end labeling (TUNEL) method and DNA gel electrophoresis. Furthermore, the expression of p53 protein was examined **immunohistochemically** in the U251 cells. After the CqTX **treatment**, the growth of all cell lines was inhibited, the fragmented DNA was observed and some cells became TUNEL

positive. The expression of p53 protein was increased in the tested U251 cells. The results suggested that CqTX induced apoptosis in these cell lines. The promotion of the p53 expression might be one mechanism of apoptosis induced by CqTX in the glioma cells.

L27 ANSWER 31 OF 36 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1986:460348 BIOSIS
DOCUMENT NUMBER: BA82:117190
TITLE: BLACK-WIDOW SPIDER VENOM-INDUCED RELEASE OF NEUROTRANSMITTERS MAMMALIAN SYNAPTOSOMES ARE STIMULATED BY A UNIQUE VENOM COMPONENT ALPHA LATROTOXIN INSECT SYNAPTOSOMES BY MULTIPLE COMPONENTS.
AUTHOR(S): KNIPPER M; MADEDDU L; BREER H; MELDOLESI J
CORPORATE SOURCE: DEP. PHARMACOL., UNIV. MILANO, VIA VANVITELLI 32, 20129 MILANO, ITALY.
SOURCE: NEUROSCIENCE, (1986) 19 (1), 55-62.
CODEN: NRSCDN. ISSN: 0306-4522.
FILE SEGMENT: BA; OLD
LANGUAGE: English
AB Synaptosomes isolated from the rat brain corpus striatum and locust head and thoracic ganglia were loaded with radioactive neurotransmitter ([3H]dopamine and [3H]acetylcholine, respectively) and then **treated** with .alpha.-latrotoxin and other fractions (fractions C, D and E of Frontali et al.8) obtained by Sephadex G200 column chromatography from black widow **spider venom** gland homogenates. As shown by sodium dodecyl sulphate-polyacrylamide gel electrophoresis, .alpha.-latrotoxin is a high Mr protein, whereas fractions C-E are mixtures of several proteins, that include small amounts of contaminating .alpha.-latrotoxin (especially in fraction C). In rat synaptosomes .alpha.-latrotoxin induced massive neurotransmitter release, and some release was induced also by high concentrations of fractions C and D. These responses were blocked almost completely by a monospecific anti-.alpha.-latrotoxin serum, indicating that they were all due to .alpha.-latrotoxin. Release of [3H]acetylcholine from locust synaptosomes was induced by the various preparations investigated. .alpha.-Latrotoxin was about 10-fold less potent in locust than in rat synaptosomes. The effects of fractions C-E tended to disappear with storage. The most active batches of fractions C and E were even more potent than .alpha.-latrotoxin, while the D fraction was approximately 5-fold less potent. The anti-.alpha.-latrotoxin antiserum inhibited part of the responses elicited by fractions C and E, but left fraction D almost unaffected. Release by D and E fractions was maintained even when Ca2+ was removed from the incubation medium. It is concluded that locust nerve endings are sensitive not only to .alpha.-latrotoxin, but also to other **venom** components: a high Mr toxin (fractions C, D), for which the name of .beta.-latrotoxin is proposed; and, possibly, a third toxin, recovered in the E fraction, that might be **immunologically** related to .alpha.-latrotoxin.

L27 ANSWER 32 OF 36 USPATFULL
ACCESSION NUMBER: 1999:159473 USPATFULL
TITLE: Method and compositions for solubilization and stabilization of polypeptides, especially proteins
INVENTOR(S): Hora, Maninder Singh, Rodeo, CA, United States
Rubinfeld, Joseph, Danville, CA, United States
Stern, Warren, Gainesville, FL, United States
Wong, Gregory J., San Leandro, CA, United States
PATENT ASSIGNEE(S): Chiron Corporation, Emeryville, CA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5997856		19991207
APPLICATION INFO.:	US 1989-373928		19890629 (7)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1988-253720, filed on 5 Oct 1988, now abandoned
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Russel, Jeffrey E.
LEGAL REPRESENTATIVE: Pochopien, Donald J., Blackburn, Robert P
NUMBER OF CLAIMS: 24
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 4 Drawing Figure(s); 4 Drawing Page(s)

LINE COUNT: 1523
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention provides a method for the solubilization and/or stabilization of polypeptides, especially proteins, using cyclodextrin selected from the group consisting of hydroxypropyl, hydroxyethyl, glucosyl, maltosyl and maltotriosyl derivatives of .beta.- and .gamma.-cyclodextrin. Solubilized and/or stabilized compositions comprising a polypeptide, especially a protein, and the selected cyclodextrin are also described.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
DETD Among the polypeptides contemplated by the present invention are **therapeutically** useful polypeptides such as anti-sera, anti-toxins and antigens. Anti-sera may include, for example, antirabies, antivenin (black widow **spider venom**), hepatitis B **immune** globulin, tetanus **immune** globulin, intravenous **immune** globulin, pertussis **immune** globulin and rabies **immune** globulin. Anti-toxins may include, for example, those for diphtheria and tetanus; Rho(D) **immune** globulin; serum components, such as 5% normal human serum albumin, 5% plasma protein fraction, 20% normal human serum albumin, 25%. . . activator, transforming growth factor (.alpha. and .beta.), tumor necrosis factor, tumor angiogenisis factor, vasoactive intestinal polypeptide and wound angiogenesis factor; **immunosuppressives**, such as RhO (D) ISG and IVGG's; thrombolytics such as urokinase, streptokinase and tissue plasminogen activator; and antigens such as. . .

L27 ANSWER 33 OF 36 USPATFULL
ACCESSION NUMBER: 1998:30684 USPATFULL
TITLE: Method and compositions for solubilization and stabilization of polypeptides, especially proteins
INVENTOR(S): Hora, Maninder Singh, Rodeo, CA, United States
Rubinfeld, Joseph, Danville, CA, United States
Stern, Warren, Gainesville, FL, United States
Wong, Gregory J., San Leandro, CA, United States
PATENT ASSIGNEE(S): Chiron Corporation, Emeryville, CA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5730969		19980324
APPLICATION INFO.:	US 1995-474178		19950607 (8)

RELATED APPLN. INFO.: Division of Ser. No. US 1989-373928, filed on 29 Jun 1989 which is a continuation-in-part of Ser. No. US 1988-253720, filed on 5 Oct 1988, now abandoned
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Russel, Jeffrey E.
LEGAL REPRESENTATIVE: Burns, Doane, Swecker & Mathis, L.L.P.
NUMBER OF CLAIMS: 79
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 4 Drawing Figure(s); 4 Drawing Page(s)
LINE COUNT: 1753
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention provides a method for the solubilization and/or stabilization of polypeptides, especially proteins, using a cyclodextrin selected from the group consisting of hydroxypropyl, hydroxyethyl, glucosyl, maltosyl and maltotriosyl derivatives of .beta.- and .gamma.-cyclodextrin. Solubilized and/or stabilized compositions comprising a polypeptide, especially a protein, and the selected cyclodextrin are also described.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
DETD Among the polypeptides contemplated by the present invention are **therapeutically** useful polypeptides such as anti-sera, anti-toxins and antigens. Anti-sera may include, for example, antirabies, antivenin (black widow **spider venom**), hepatitis B **immune** globulin, tetanus **immune** globulin, intravenous **immune** globulin, pertussis **immune** globulin and rabies **immune** globulin. Anti-toxins may include, for example, those for diphtheria and tetanus; Rho(D) **immune** globulin; serum components, such as 5% normal

human serum albumin, 5% plasma protein fraction, 20% normal human serum albumin, 25%. . . activator, transforming growth factor (.alpha. and .beta.), tumor necrosis factor, tumor angiogenisis factor, vasoactive intestinal polypeptide and wound angiogenesis factor; **immunosuppressives**, such as RHO (D) ISG and IVGG's; thrombolytics such as urokinase, streptokinase and tissue plasminogen activator; and antigens such as. . .

L27 ANSWER 34 OF 36 USPATFULL

ACCESSION NUMBER:	2000:174351 USPATFULL			
TITLE:	Representations of bimolecular interactions			
INVENTOR(S):	Gershoni, Jonathan M., Rehovot, Israel Enshel, David, Givatayim, Israel			
PATENT ASSIGNEE(S):	Ramot University Authority for Applied Research & Industrial Development Ltd., Tel Aviv, Israel (non-U.S. corporation)			
	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6165722		20001226	
	WO 9820159		19980514	
APPLICATION INFO.:	US 1999-297669		19990506	(9)
	WO 1997-IL354		19971104	
			19990506	PCT 371 date
			19990506	PCT 102(e) date
	NUMBER		DATE	
PRIORITY INFORMATION:	IL 1996-119587		19961107	
DOCUMENT TYPE:	Utility			
FILE SEGMENT:	Granted			
PRIMARY EXAMINER:	Jones, W. Gary			
ASSISTANT EXAMINER:	Forman, B J			
LEGAL REPRESENTATIVE:	Friedman, Mark M.			
NUMBER OF CLAIMS:	34			
EXEMPLARY CLAIM:	1			
LINE COUNT:	1587			

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A method of preparing a bimolecular interaction library for a first biological unit and for a second biological unit, each of the first and second biological units having a corresponding genetic material, the method comprising the steps of: (a) preparing a first fragment from the genetic material corresponding to the first biological unit; (b) preparing a first phage library having a first selection marker with the first fragment, such that a first peptide is displayed by the first phage library; (c) preparing a second fragment from the genetic material corresponding to the second biological unit; (d) preparing a second phage library having a second selection marker with the second fragment, such that a second peptide is displayed by the second phage library; (e) mixing the first phage library and the second phage library; and (f) co-selecting co-selected phages from the first phage library and from the second phage library by the first selection marker and the second selection marker when a selection process yields a positive result, such that the selection process yields the positive result only when the first peptide and the second peptide interact, and such that the bimolecular interaction library is formed from the co-selected phages.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

DETD . . . section above, an active vaccine causes at least one epitope of a first biological unit to be presented to the **immune** system of an organism, which is the organism to be vaccinated. The first biological unit is typically, but not necessarily,. . . bacterium, yeast or parasite. The first biological unit could also be a toxic substance, such as a snake, insect or **spider venom** toxin, a plant toxin or even a synthetic toxin. Alternatively, the first biological unit could even be a part of. . . as a cancer cell, or a portion thereof, for example. It should be noted, however, that in the case of **autoimmune** reactions, **treatment** of cancerous cells, or cells exhibiting inappropriate activity for the stage in the life cycle of the organism, the first. . . a cell exhibiting inappropriate activity for the stage in the life cycle of the organism. Alternatively, in the case of **autoimmune** reactions such as myasthenia gravis, lupus erythematosus or rheumatoid arthritis, the

"epitope of the first organism" is normally expressed, but the **immune** reaction is inappropriate. In any case, the terms "first" and "second" organism are used below for clarity, it being understood. . .

L27 ANSWER 35 OF 36 USPATFULL
ACCESSION NUMBER: 2000:12973 USPATFULL
TITLE: Cytoprotective compounds
INVENTOR(S): Franson, Richard C., Richmond, VA, United States
Ottenbrite, Raphael M., Midlothian, VA, United States
PATENT ASSIGNEE(S): Virginia Commonwealth University, Richmond, VA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6020510		20000201
APPLICATION INFO.:	US 1998-17511		19980202 (9)

RELATED APPLN. INFO.: Continuation of Ser. No. US 1996-632030, filed on 15 Apr 1996, now patented, Pat. No. US 5859271
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Reamer, James H.
LEGAL REPRESENTATIVE: Jones & Askew LLP
NUMBER OF CLAIMS: 31
EXEMPLARY CLAIM: 1
LINE COUNT: 1891
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention provides compositions and methods for protecting cells from injury due to intrinsic membrane lysis, oxidation and/or invasion by destructive agents. Even more particularly, the present invention provides compositions and methods for treating or prophylactically inhibiting phospholipase mediated injury, injury due to oxidation, and inflammation. In a very specific sense, this invention provides compositions and methods of making these compositions that are inhibitors of phospholipase.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
SUMM Another object of the present invention is to provide oral and topical **treatments** comprising administration of an effective amount of the compositions of the present invention, for a variety of conditions, such conditions. . . including septic shock, anaphylactic shock, anaphylactic shock resulting from radiocontrast administration, and shock resulting from bacterial infections; bacterial infections; uremia; **autoimmune** disorders; parasitic infections including, but not limited to, malaria; inflammation including allergic inflammation; skin inflammation, itching, and other dermatologic disorders. . . poison ivy, poison oak, poison sumac; bites of insects including, but not limited to, mosquitos, fire ants, chiggers, ticks, bees, **spiders**, fleas and flies; bites of reptiles, especially **venomous** reptiles, amphibians, and other animals; contact with various animals with **venom** on their skin such as poisonous frogs; pruritis associated with local dermatologic or systemic disease; prevention of tissue ischemia including. . .

L27 ANSWER 36 OF 36 USPATFULL
ACCESSION NUMBER: 1999:4922 USPATFULL
TITLE: Cytoprotective compounds
INVENTOR(S): Franson, Richard C., Richmond, VA, United States
Ottenbrite, Raphael M., Midlothian, VA, United States
PATENT ASSIGNEE(S): Virginia Commonwealth University, Richmond, VA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5859271		19990112
APPLICATION INFO.:	US 1996-632030		19960415 (8)

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Reamer, James H.
LEGAL REPRESENTATIVE: Jones & Askew, LLP
NUMBER OF CLAIMS: 12
EXEMPLARY CLAIM: 1
LINE COUNT: 1803

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention provides compositions and methods for protecting cells from injury due to intrinsic membrane lysis, oxidation and/or invasion by destructive agents. Even more particularly, the present invention provides compositions and methods for treating or prophylactically inhibiting phospholipase mediated injury, injury due to oxidation, and inflammation. In a very specific sense, this invention provides compositions and methods of making these compositions that are inhibitors of phospholipase.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
SUMM Another object of the present invention is to provide oral and topical **treatments** comprising administration of an effective amount of the compositions of the present invention, for a variety of conditions, such conditions. . . including septic shock, anaphylactic shock, anaphylactic shock resulting from radiocontrast administration, and shock resulting from bacterial infections; bacterial infections; uremia; **autoimmune** disorders; parasitic infections including, but not limited to, malaria; inflammation including allergic inflammation; skin inflammation, itching, and other dermatologic disorders. . . poison ivy, poison oak, poison sumac; bites of insects including, but not limited to, mosquitos, fire ants, chiggers, ticks, bees, **spiders**, fleas and flies; bites of reptiles, especially **venomous** reptiles, amphibians, and other animals; contact with various animals with **venom** on their skin such as poisonous frogs; pruritis associated with local dermatologic or systemic disease; prevention of tissue ischemia including. . .

=> FIL MEDL CAPL BIOSIS USPATF

=> s l15 (s) immun?
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L86 (S) IMMUN?'
L28 17 L15 (S) IMMUN?

=> focus
PROCESSING COMPLETED FOR L28
L29 17 FOCUS L28 1-

=> d ibib abs kwic 1-5

L29 ANSWER 1 OF 17 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:98561 CAPLUS
DOCUMENT NUMBER: 132:137381
TITLE: Preparation of oxazolo, thiazolo and selenazolo[4,5-c]quinolin-4-amines as immunomodulators and for inducing cytokine biosynthesis
INVENTOR(S): Gerster, John F.; Lindstrom, Kyle J.; Marszalek, Gregory J.; Merrill, Bryon A.; Mickelson, John W.; Rice, Michael J.
PATENT ASSIGNEE(S): 3M Innovative Properties Company, USA
SOURCE: PCT Int. Appl., 109 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

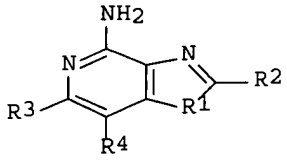
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000006577	A1	20000210	WO 1999-US17027	19990728
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6110929	A	20000829	US 1999-361544	19990727
AU 9951331	A1	20000221	AU 1999-51331	19990728
EP 1100802	A1	20010523	EP 1999-935968	19990728

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

BR 9912448	A	20011009	BR 1999-12448		19990728
US 6323200	B1	20011127	US 2000-593434		20000614
NO 2001000497	A	20010327	NO 2001-497		20010129
PRIORITY APPLN. INFO.:			US 1998-94346	P	19980728
			US 1999-361544	A	19990727
			WO 1999-US17027	W	19990728

OTHER SOURCE(S): MARPAT 132:137381

GI



I

AB The title compds. [R1 = O, S, Se; R2 = H, alkyl, alkyl-OH, etc.; R3, R4 = H, halo, haloalkyl, etc.] which are immunomodulators and induce cytokine biosynthesis, including interferon-.alpha. and/or tumor necrosis factor-.alpha. biosynthesis, and inhibit the T-helper-type 2 immune response, were prepd. E.g., a multi-step synthesis of I [R1 = S; R2 = Me; R3R4 = CH:CHCH:CH] was given. Biol. data for compds. I were presented. The compds. I are further useful in the treatment of viral and neoplastic diseases.

REFERENCE COUNT: 4

REFERENCE(S):
(1) American Cyanamid Co; WO 9816514 A 1998 CAPLUS
(2) American Home Products Corp; EP 0055248 A 1982 CAPLUS
(3) Minnesota Mining And Manufacturing Co; WO 9305042 A 1993 CAPLUS
(4) Tsung-Ying, S; US 4038396 A 1977

IT **256922-53-9P**
RL: BAC (Biological activity or effector, except adverse); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of oxazolo, thiazolo and selenazolo[4,5-c]quinolin-4-amines as **immunomodulators** and for inducing cytokine biosynthesis)

IT **256922-47-1P** 256922-48-2P 256922-49-3P 256922-50-6P, Thiazolo[4,5-c]quinolin-4-amine **256922-51-7P** 256922-52-8P 256922-54-0P 256922-55-1P **256922-56-2P** 256922-57-3P 256922-58-4P 256922-59-5P 256922-60-8P 256922-61-9P 256922-62-0P 256922-63-1P 256922-64-2P 256922-65-3P 256922-66-4P 256922-67-5P 256922-68-6P 256922-69-7P 256922-70-0P 256922-71-1P 256922-72-2P 256922-73-3P 256922-74-4P 256922-75-5P 256922-76-6P 256922-77-7P 256922-78-8P 256922-79-9P 256922-80-2P 256922-81-3P 256922-82-4P 256922-83-5P 256922-84-6P 256922-85-7P 256922-86-8P 256923-68-9P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of oxazolo, thiazolo and selenazolo[4,5-c]quinolin-4-amines as **immunomodulators** and for inducing cytokine biosynthesis)

L29 ANSWER 2 OF 17 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 2001:431847 CAPLUS

DOCUMENT NUMBER: 135:24716

TITLE: Formulations and methods for treatment of mucosal associated conditions with an immune response modifier

INVENTOR(S): Skwierczynski, Raymond D.; Phares, Kenneth R.; Miller, Richard L.; Li, Zheng Jane; Jozwiakowski, Michael J.; Busch, Terri F.

PATENT ASSIGNEE(S): 3M Innovative Properties Company, USA

SOURCE: U.S., 17 pp.
CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6245776	B1	20010612	US 2000-479578	20000107

AB Immune response modifier (IRM) compds. selected from the group consisting of imidazoquinoline amines, imidazopyridine amines, 6,7-fused cycloalkylimidazopyridine amines, 1,2-bridged imidazoquinoline amines, thiazolo- and oxazolo-quinolinamines and pyridinamines, imidazonaphthyridine and tetrahydroimidazonaphthyridine amines, are useful for the treatment of conditions at and below the mucosal surfaces by administering a therapeutically effective amt. of such compds. to the mucosal surface. Novel pharmaceutical formulations are provided. In one embodiment, the pharmaceutical formulations are advantageous for treatment of cervical conditions such as cervical dysplasias including cervical intraepithelial neoplasias. A vaginal cream contained imiquimod 5, isostearic acid 25, benzyl alc. 2, cetyl alc. 2.2, stearyl alc. 3.1, white petrolatum 3, polysorbate-60 3.4, sorbitan monostearate 0.6, glycerin 0.2, methylparaben 0.2, propylparaben 0.02, water 52.98, and xanthan gum 0.5 %.

REFERENCE COUNT: 55
REFERENCE(S):
(1) Andre; US 4988815 1991 CAPLUS
(2) Anon; WO 93-09119 1993 CAPLUS
(3) Anon; JP 09-208584 1997 CAPLUS
(4) Anon; WO 97-41884 1997 CAPLUS
(5) Anon; WO 97-48704 1997 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

IT 94-13-3, Propylparaben 99-76-3, Methylparaben 110-44-1, Sorbic acid 2724-58-5, Isostearic acid 26266-58-0, Span 85 **99011-02-6**, Imiquimod 106392-12-5, Poloxamer 188 **144875-48-9**, 4-Amino-2-ethoxymethyl-.alpha.,.alpha.-dimethyl-1H-imidazo[4,5-c]quinoline-1-ethanol 151687-96-6, Carbopol 974p
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(mucosal pharmaceuticals contg. **immune** response modifiers and fatty acids and preservatives)

L29 ANSWER 3 OF 17 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:676400 CAPLUS
DOCUMENT NUMBER: 134:36792
TITLE: Adjuvant Activities of Immune Response Modifier R-848: Comparison with CpG ODN
AUTHOR(S): Vasilakos, John P.; Smith, Rose M. A.; Gibson, Sheila J.; Lindh, Jana M.; Pederson, Linda K.; Reiter, Michael J.; Smith, Michael H.; Tomai, Mark A.
CORPORATE SOURCE: Department of Pharmacology, 3M Pharmaceuticals, St. Paul, MN, 55144, USA
SOURCE: Cell. Immunol. (2000), 204(1), 64-74
CODEN: CLIMB8; ISSN: 0008-8749
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB R-848 and imiquimod belong to a class of immune response modifiers that are potent inducers of cytokines, including IFN-.alpha., TNF-.alpha., IL-12, and IFN-.gamma.. Many of these cytokines can affect the acquired immune response. This study examines the effects of R-848 on aspects of acquired immunity, including Ig secretion, in vivo cytokine prodn., and Ag-specific T cell cytokine prodn. Results are compared with those of Th1 CpG ODN. R-848 and CpG ODN are effective at skewing immunity in the presence of Alum toward a Th1 Ab response (IgG2a) and away from a Th2 Ab response (IgE). R-848 and CpG ODN are also capable of initiating an immune response in the absence of addnl. adjuvant by specifically enhancing IgG2a levels. Both R-848 and imiquimod showed activity when given s.c. or orally, indicating that the compd. mechanism was not through generation of a depot effect. Although CpG ODN behaves similarly to R-848, CpG ODN has a distinct cytokine profile, is more effective than R-848 when given with Alum in the priming dose, and is active only when given by the same route as the Ag. The mechanism of R-848's adjuvant activity is linked to cytokine prodn., where increases in IgG2a levels are assocd. with IFN-.alpha., TNF-.alpha., IL-12, and IFN-.gamma. induction, and decreases in IgE levels are assocd. with IFN-.alpha. and TNF-.alpha.. Imiquimod also enhances IgG2a prodn. when given with Ag. The above results suggest that the imidazoquinolines R-848 and imiquimod may be

attractive compds. for use as vaccine adjuvants and in inhibiting pathol. responses mediated by Th2 cytokines. (c) 2000 Academic Press.

REFERENCE COUNT: 41

REFERENCE(S):
(1) Ahonen, C; Cell Immunol 1999, V197, P62 CAPLUS
(2) Ballas, Z; J Immunol 1996, V157, P1840 CAPLUS
(3) Bernstein, D; J Infect Dis 1993, V167, P731 CAPLUS
(4) Bernstein, D; Vaccine 1995, V13, P72 CAPLUS
(6) Broide, D; J Immunol 1998, V161, P7054 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

IT 2382-65-2 **144875-48-9**, r-848
RL: BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(adjuvant activities of **immune** response modifier R-848: comparison with CpG ODN)

IT **99011-02-6**, Imiquimod
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(adjuvant activities of **immune** response modifier R-848: comparison with CpG ODN and)

L29 ANSWER 4 OF 17 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 2000:475527 CAPLUS
DOCUMENT NUMBER: 133:94545
TITLE: Formulations and methods for treatment of mucosal associated conditions with an immune response modifier
INVENTOR(S): Phares, Kenneth; Li, Jane Z.; Jozwiakowski, Michael J.; Miller, Richard L.; Skwierczynski, Raymond D.; Busch, Terri F.
PATENT ASSIGNEE(S): M Innovative Properties Company, USA
SOURCE: PCT Int. Appl., 54 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000040228	A2	20000713	WO 2000-US370	20000107
WO 2000040228	A3	20010405		
W: AE, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1140091	A2	20011010	EP 2000-905559	20000107
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 2000007435	A	20011204	BR 2000-7435	20000107
NO 2001003230	A	20010910	NO 2001-3230	20010627

PRIORITY APPLN. INFO.: US 1999-115253 P 19990108
WO 2000-US370 W 20000107

AB Immune response modifier (IRM) compds., imidazoquinoline amines, imidazopyridine amines, 6,7-fused cycloalkylimidazopyridineamines, 1,2-bridged imidazoquinoline amines, thiazolo- and oxazolo- quinolinamines and pyridinamines, imidazonaphthyridine and tetrahydroimidazonaphthyridine amines, useful for the treatment of conditions at and below the mucosal surfaces by administering a therapeutically effective amt. of such compds. to the mucosal surface. Novel pharmaceutical formulations are provided. In 1 embodiment, the pharmaceutical formulations are advantageous for treatment of cervical conditions such as cervical dysplasias including cervical intraepithelial neoplasias. A formulation contained isostearic acid 15.00, imiquimod 0.10, sorbitan trioleate 1.00, propylene glycol 5.00, sorbic acid 0.15, methylparaben 0.20, purified water 75.00, disodium edetate 0.05, Poloxamer-188 2.50, Carbomer-974P 1.00 and NaOh qs to 100%.

IT **99011-02-6**, Imiquimod
RL: BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(formulations for treatment of mucosal-assocd. conditions with **immune** response modifier)

IT 110-44-1, Sorbic acid 30399-84-9, Isostearic acid **144875-48-9**,
4-Amino-2-ethoxymethyl-.alpha.,.alpha.-dimethyl-1H-imidazo[4,5-c]quinoline-
1-ethanol 151687-96-6, Carbopol 974P
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(formulations for treatment of mucosal-assocd. conditions with
immune response modifier)

L29 ANSWER 5 OF 17 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:268359 CAPLUS
DOCUMENT NUMBER: 128:317256
TITLE: Imidazoquinoline amine and imidazopyridine amine immune response modifier compounds for treatment of TH2-mediated and related diseases
INVENTOR(S): Tomai, Mark A.; Hammerbeck, David M.; Swingle, Karl F.
PATENT ASSIGNEE(S): Minnesota Mining and Manufacturing Co., USA
SOURCE: PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9817279	A1	19980430	WO 1997-US19990	19971024
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9851641	A1	19980515	AU 1998-51641	19971024
AU 724042	B2	20000907		
EP 938315	A1	19990901	EP 1997-946484	19971024
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE, PT, IE				
JP 2001502699	T2	20010227	JP 1998-519752	19971024
NO 9901908	A	19990421	NO 1999-1908	19990421
US 6200592	B1	20010313	US 2000-528620	20000320

PRIORITY APPLN. INFO.:
US 1996-29301 P 19961025
US 1997-45331 P 19970501
US 1997-957192 A3 19971024
WO 1997-US19990 W 19971024

OTHER SOURCE(S): MARPAT 128:317256
AB Immune response modifier compds. -- imidazoquinoline amines, imidazopyridine amines, 6,7-fused cycloalkylimidazopyridine amines, and 1,2-bridged imidazoquinoline amines -- are useful for the treatment of TH2 mediated diseases by administering a therapeutically effective amt. of such compds. in order to inhibit TH2 immune response, suppress IL-4/IL-5 cytokine induction and eosinophilia, as well as enhance TH1 immune response.
IT 233-56-7D, 1H-Imidazo[4,5-c]quinoline, amine derivs. 272-97-9D, 1H-Imidazo[4,5-c]pyridine, amine derivs. **99011-02-6** 99011-16-2 **144875-48-9**
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(imidazoquinoline amine and imidazopyridine amine **immune** response modifier compds. for treatment of TH2-mediated and related diseases)

=> s th2 mediat?
L30 446 TH2 MEDIAT?

=> s l30 (s) l111
L31 0 L30 (S) LL11

=> s l30 (s) l11
L32 0 L30 (S) LL1

=> d ibib abs kwic l29 6-17

L29 ANSWER 6 OF 17 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2001:561869 CAPLUS
DOCUMENT NUMBER: 135:313221
TITLE: Application of a topical immune response modifier, resiquimod gel, to modify the recurrence rate of recurrent genital herpes: A pilot study
AUTHOR(S): Spruance, Spotswood L.; Tyring, Stephen K.; Smith, Michael H.; Meng, Tze-Chiang
CORPORATE SOURCE: Department of Medicine, School of Medicine, University of Utah, Salt Lake City, UT, 84132, USA
SOURCE: J. Infect. Dis. (2001), 184(2), 196-200
CODEN: JIDIAQ; ISSN: 0022-1899
PUBLISHER: University of Chicago Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Resiquimod (R-848), a topically active immune response modifier, induced prodn. of interferon-.alpha. and interleukin-12 in cultured blood mononuclear cells and decreased genital herpes recurrences in an animal model. In this study, 52 patients with frequently recurrent genital herpes applied topical resiquimod gel 0.01% (twice or thrice weekly) or 0.05% (once or twice weekly) or vehicle gel to herpes lesions for 3 wk. During the 6-mo observation period after treatment, median days to first recurrence in the pooled resiquimod group was 169 days, compared with 57 days for the vehicle group (P =.0058). In all, 32% of resiquimod-treated patients completed the observation period without a recurrence, compared with 6% of vehicle-treated patients (P =.039). Resiquimod 0.05% twice weekly produced dose-limiting inflammation at the lesion sites, but the other regimens were well tolerated. Application of resiquimod to genital herpes lesions appeared to reduce the frequency of recurrences.
REFERENCE COUNT: 14
REFERENCE(S): (2) Bernstein, D; J Infect Dis 1993, V167, P731 CAPLUS
(3) Bernstein, D; J Infect Dis 2001, V183, P844 CAPLUS
(8) Reitano, M; J Infect Dis 1998, V178, P603 CAPLUS
(9) Reiter, M; J Leukoc Biol 1994, V55, P234 CAPLUS
(11) Straus, S; J Infect Dis 1997, V176, P1129 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT
IT **144875-48-9**, Resiquimod
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(application of topical **immune** response modifier, resiquimod gel, to modify recurrence rate of recurrent genital herpes)

L29 ANSWER 7 OF 17 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2001:383665 CAPLUS
DOCUMENT NUMBER: 135:235754
TITLE: A review of the applications of imiquimod: A novel immune response modifier
AUTHOR(S): Syed, Tanweer A.
CORPORATE SOURCE: Department of Dermatology, University of California San Francisco, San Francisco, CA, USA
SOURCE: Expert Opin. Pharmacother. (2001), 2(5), 877-882
CODEN: EOPHF7; ISSN: 1465-6566
PUBLISHER: Ashley Publications Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 37 refs. Imiquimod [1-(2-methylpropyl)-1 H-imidazo(4,5-clquinolin-4-amine)] and its analogs are a class of non-nucleoside imidazoquinolinamines (heterocyclic amine) that activate the immune system through localised induction of cytokines, such as IFN-.alpha., -.beta. and a no. of endogenous interleukins. The exact mechanism of its actions are still unexplored, although when tested in a no. of cell culture systems, imiquimod demonstrated no inherent antiviral or antiproliferative activity in vitro, whereas, due to its reported ability to produce onsite stimulation and secretion of cytokines in various in vivo studies, such types of immune response modifiers have been shown to cause diverse biol. functions, involving immunoregulatory, antiviral, antiproliferative and antitumor activities. These data support a rational justification to consider imiquimod as an innovative topical agent to treat various cutaneous diseases. Since its synthesis in 1980, several studies using animal models and human subjects have been reported substantiating its usefulness as a treatment option for various skin disorders such as genital warts, genital herpes, molluscum contagiosum, basal cell carcinoma and psoriasis. Imiquimod is insol. in water but in

most of the clin. studies its incorporation from 1-5% by wt. in an oil-into-water cream emulsion has been reported as being well-tolerated with mild-to-moderate drug-related side effects, such as itching, burning sensation, pain, erythema, erosion and edema. As a potent immune response modifier and an agent stimulating cell-mediated immune responses, imiquimod appears to be a promising drug to treat many skin disorders, infections and neoplasms.

REFERENCE COUNT: 37
REFERENCE(S):
(4) Beutner, K; Antimicrob Agents Chemother 1998, V42, P789 CAPLUS
(7) Bottrel, R; Antimicrob Agents Chemother 1999, V43, P856 CAPLUS
(9) Chollet, J; Pharm Dev Technol 1999, V4, P35 CAPLUS
(14) Gibson, S; Interferon and Cytokine Res 1995, V15, P537 CAPLUS
(15) Imbertson, L; J Invest Dermatol 1998, V110, P734 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

IT **99011-02-6**, Imiquimod
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(review of applications of imiquimod: a novel **immune** response modifier)

L29 ANSWER 8 OF 17 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2001:222426 CAPLUS
DOCUMENT NUMBER: 135:75442
TITLE: The Immune Response Modifier Resiquimod Mimics CD40-Induced B Cell Activation
AUTHOR(S): Bishop, Gail A.; Ramirez, Luis M.; Baccam, Mekhine; Busch, Lisa K.; Pederson, Linda K.; Tomai, Mark A.
CORPORATE SOURCE: Department of Microbiology, 3M Pharmaceuticals, St. Paul, MN, 55144, USA
SOURCE: Cell. Immunol. (2001), 208(1), 9-17
CODEN: CLIMB8; ISSN: 0008-8749
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Members of the imidazoquinoline mol. family, including imiquimod and resiquimod (R-848), have potent antiviral and antitumor activities. Imiquimod cream (5%) (Aldara) is currently indicated for treatment of external genital and perianal warts. Previous characterization of these compds. has focused upon their ability to activate monocytes and dendritic cells, but recent studies have shown that resiquimod also stimulates B lymphocytes to proliferate and express an activated phenotype. This suggests that resiquimod could potentially serve as an effective vaccine adjuvant in stimulating a humoral immune response. This study shows that resiquimod mimics effects of the T-dependent CD40 signal in both mouse and human B cell lines. Resiquimod, like CD40, stimulates antibody secretion, cytokine prodn., protection from apoptosis, and CD80 upregulation. In addn., it shows synergy with signals delivered by the B cell antigen receptor and heightens CD40-mediated B cell activation, demonstrating that resiquimod can enhance antigen-specific responses in B lymphocytes. (c) 2001 Academic Press.

REFERENCE COUNT: 52
REFERENCE(S):
(1) Arch, R; Genes Dev 1998, V12, P2821 CAPLUS
(2) Baccam, M; Eur J Immunol 1999, V29, P3855 CAPLUS
(4) Bishop, G; Eur J Immunol 1995, V25, P1230 CAPLUS
(5) Bishop, G; J Immunol 1991, V147, P1107 CAPLUS
(6) Bishop, G; J Immunol 1993, V150, P2565 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

IT **144875-48-9**, Resiquimod
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BIOL (Biological study); PROC (Process)
(**immune** response modifier resiquimod mimics CD40-induced B cell activation)

L29 ANSWER 9 OF 17 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:825812 CAPLUS
DOCUMENT NUMBER: 134:125717
TITLE: Molecular mechanisms of B lymphocyte activation by the immune response modifier R-848

AUTHOR(S): Bishop, Gail A.; Hsing, Yina; Hostager, Bruce S.; Jalukar, Sangita V.; Ramirez, Luis M.; Tomai, Mark A.
CORPORATE SOURCE: Departments of Microbiology and Internal Medicine, Graduate Program in Immunology, Veterans Administration Medical Center, Iowa City, IA, 52242, USA
SOURCE: J. Immunol. (2000), 165(10), 5552-5557
CODEN: JOIMA3; ISSN: 0022-1767
PUBLISHER: American Association of Immunologists
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The imidazoquinoline R-848, originally identified as a highly effective antiviral agent, has recently been shown to be capable of potent B lymphocyte activation. The B cell-activating properties of R-848 are strikingly similar to the effects of the CD40 ligand CD154. The present study demonstrates that this similarity extends to the intracellular signaling pathways triggered by the compd., although both overlapping and distinct mechanisms of signaling were seen. Like CD40 ligation, R-848 stimulated activation of the stress-activated protein kinases c-Jun kinase and p38 and activated the NF-.kappa.B family of transcription factors. Both R-848- and CD40-mediated B cell differentiation were dependent upon NF-.kappa.B activation, although the relative importance of individual NF-.kappa.B family members appeared to differ between R-848- and CD40-mediated signals. Both signals were partially dependent upon induction of TNF-.alpha. and IL-6, and the cytoplasmic adaptor mol. TNF receptor-assocd. factor 2 is involved in both R-848- and CD40-mediated differentiation.

REFERENCE COUNT: 54
REFERENCE(S):
(1) Ahonen, C; Cell Immunol 1999, V197, P62 CAPLUS
(2) Arch, R; Genes Dev 1998, V12, P2821 CAPLUS
(3) Baeuerle, P; Annu Rev Immunol 1994, V12, P141 CAPLUS
(4) Baker, S; Oncogene 1996, V12, P1 CAPLUS
(5) Bernstein, D; Antimicrob Agents Chemother 1989, V33, P1511 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

IT **144875-48-9**, R-848
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(mol. mechanisms of B lymphocyte activation by the **immune** response modifier R-848)

L29 ANSWER 10 OF 17 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:726508 CAPLUS
DOCUMENT NUMBER: 134:289758
TITLE: Immune-response modifiers: A new paradigm in the treatment of human papillomavirus
AUTHOR(S): Tyring, Stephen K.
CORPORATE SOURCE: Departments of Dermatology, Microbiology / Immunology, and Internal Medicine, University of Texas Medical Branch, Galveston, TX, USA
SOURCE: Curr. Ther. Res. (2000), 61(9), 584-596
CODEN: CTCEA9; ISSN: 0011-393X
PUBLISHER: Excerpta Medica, Inc.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 53 refs. Human papillomavirus (HPV) infection is common across all races and socioeconomic groups and is prevalent throughout the world. A variety of HPV-assocd. diseases exist-from the highly prevalent but benign verruca vulgaris to cervical cancer, a leading cause of cancer death in women worldwide. Cellular rather than humoral immunity appears to be central to the control and eradication of HPV. It is likely that the HPV proteins responsible for viral replication and promotion of replication within the tissues are the targets of antigen-specific T cells. However, the host is slow to mount a therapeutic immune response to these proteins naturally, possibly because HPV has developed a means of preventing its viral antigens from being presented to the host's immune system. HPV infection is nonlytic; therefore, the viral antigen may not be released to the dendritic (antigen-presenting) cells. In addn., no local inflammation or proinflammatory cytokine prodn. is assocd. with HPV infection. This review explores the role of the immune response in combating HPV infection and the mechanism of action by which imiquimod modifies this response. The optimal treatment for HPV infection would be

one that produces a strong virus-specific immune response through the induction of appropriate local inflammation and of those cytokines necessary for HPV-specific immunity. Studies have shown that topical application of imiquimod, an immune-response modifier, induces local cytokine prodn. and reduces HPV load in patients with external genital warts.

REFERENCE COUNT: 53

REFERENCE(S):
(1) Arany, I; J Interferon Cytokine Res 1996, V16, P453 CAPLUS
(3) Beutner, K; Am J Med 1997, V102, P28 CAPLUS
(4) Beutner, K; Antimicrob Agents Chemother 1998, V42, P789 CAPLUS
(24) Frazer, I; Curr Opin Immunol 1996, V8, P484 CAPLUS
(28) Harrison, C; Antimicrob Agents Chemother 1994, V38, P2059 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

IT **99011-02-6**, Imiquimod
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**immune**-response modifiers in treatment of human papillomavirus)

L29 ANSWER 11 OF 17 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:573917 CAPLUS
DOCUMENT NUMBER: 133:161581
TITLE: Maturation of dendritic cells with imidazoquinoline type immune response modifying compounds
INVENTOR(S): Tomai, Mark A.; Vasilakos, John P.; Ahonen, Cory L.
PATENT ASSIGNEE(S): 3M Innovative Properties Company, USA
SOURCE: PCT Int. Appl., 52 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000047719	A2	20000817	WO 2000-US757	20000112
WO 2000047719	A3	20001130		
W: AE, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1153122	A2	20011114	EP 2000-903269	20000112
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
NO 2001003875	A	20011008	NO 2001-3875	20010808

PRIORITY APPLN. INFO.: US 1999-248439 A 19990211
WO 2000-US757 W 20000112

OTHER SOURCE(S): MARPAT 133:161581

AB A method of inducing the maturation of dendritic cells involves stimulating immature dendritic cells with an imidazoquinoline type immune response modifying compd. Dendritic cells that have been matured in this manner display increased antigen presenting ability and may be used as immunotherapeutic agents. R-848 induced monocyte-derived dendritic cell cytokine and chemokine secretion characteristic of dendritic cell maturation.

IT **144875-48-9**
RL: BAC (Biological activity or effector, except adverse); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(maturation of dendritic cells with imidazoquinoline type **immune** response modifying compds.)

L29 ANSWER 12 OF 17 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:444425 CAPLUS

DOCUMENT NUMBER: 134:99149
TITLE: Stimulation of the innate immune system: a paradigm for the future identification of disease modifying agents to treat asthma and allergic diseases
AUTHOR(S): Williams, Robert J.
CORPORATE SOURCE: Aventis Pharmaceuticals, Essex, RM10 7XS, UK
SOURCE: Emerging Ther. Targets (2000), 4(3), 313-321
CODEN: ETTAF7; ISSN: 1460-0412
PUBLISHER: Ashley Publications Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review and discussion with 65 refs. Asthma and allergic diseases in general have reached epidemic proportions in the developed world. Current asthma therapy relies heavily on the prophylactic use of anti-inflammatory corticosteroids administered by inhalation. However, concerns remain regarding the side effect profile of these agents and also their efficacy in controlling disease in many patients. Epidemiol. studies have suggested a link between lack of exposure to bacteria and the rising incidence of allergic diseases. Furthermore, recent animal studies have clearly shown that administration of bacteria or bacterial components, notably DNA, can suppress allergen-induced lung inflammation. Most noteworthy is the observation that the anti-inflammatory effects of bacterial DNA sequences contg. unmethylated CG dinucleotides (CpG motifs) can be long lasting. This observation has led to the suggestion that therapies based on these or related mols. may potentially be disease modifying. The mechanisms invoked to explain this phenomenon relate to stimulation of cytokine prodn., notably IL-12, by cells of the innate immune system. This appears to lead to generation of Th1- rather than Th2-type immunol. memory to potential allergens and also the generation of suppresser T-lymphocyte subsets. Data reported for compds. of the imidazoquinoline class has demonstrated that it is possible to identify low mol. wt. compds. with similar anti-allergic properties. Development of our understanding of the cellular and mol. basis for the anti-allergic properties of bacterially-derived immunostimulants and related mols. is likely to lead to the identification of new, potentially disease modifying therapies for the treatment of asthma and allergic diseases.

REFERENCE COUNT: 65
REFERENCE(S): (1) Abbas, A; Cell 2000, V100, P129 CAPLUS
(2) Auci, D; Immunol Inv 1998, V27, P105 CAPLUS
(4) Bendigs, S; Eur J Immunol 1999, V29, P1209 CAPLUS
(5) Broide, D; J Immunol 1998, V161, P7054 CAPLUS
(6) Cardon, L; Proc Natl Acad Sci USA 1994, V91, P3799 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

IT **144875-48-9**, s28463 151751-58-5, s27609
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(stimulation of the innate **immune** system and modifying agents to treat asthma and allergic diseases)

L29 ANSWER 13 OF 17 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:715919 CAPLUS
DOCUMENT NUMBER: 132:44663
TITLE: Dendritic cell maturation and subsequent enhanced T-cell stimulation induced with the novel synthetic immune response modifier R-848
AUTHOR(S): Ahonen, Cory L.; Gibson, Sheila J.; Smith, Rose M.; Pederson, Linda K.; Lindh, Jana M.; Tomai, Mark A.; Vasilakos, John P.
CORPORATE SOURCE: Department of Pharmacology, 3M Pharmaceuticals, St. Paul, MN, 55144-1000, USA
SOURCE: Cell. Immunol. (1999), 197(1), 62-72
CODEN: CLIMB8; ISSN: 0008-8749
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Agents that enhance dendritic cell maturation can enhance T-cell activation and therefore may improve the efficiency of vaccines or improve cellular immunotherapy. Previously, we demonstrated that a novel low-mol.-wt. synthetic immune response modifier, R-848, induces IL-12 and IFN-.alpha. secretion from monocytes and macrophages. Here we report that R-848 induces the maturation of human monocyte-derived dendritic cells. Characteristic of dendritic cell maturation, R-848 treatment induces cell surface expression of CD83 and increases cell surface expression of CD80,

CD86, CD40, and HLA-DR. Addnl., R-848 induces cytokine (IL-6, IL-12, TNF-.alpha., IFN-.alpha.) and chemokine (IL-8, MIP-1.alpha., MCP-1) secretion from dendritic cells. Most significantly, R-848 enhances dendritic cell antigen presenting function, as measured by increased T-cell proliferation and T-cell cytokine secretion in both allogeneic and autologous T-cell systems. Consequently, low-mol.-wt. synthetic mols. such as R-848 and its derivs. may be useful as vaccine adjuvants or as ex vivo stimulators of dendritic cells for cellular immunotherapy. (c) 1999 Academic Press.

REFERENCE COUNT: 45

REFERENCE(S):
(2) Bender, A; J Immunol Methods 1996, V196, P121 CAPLUS
(3) Caux, C; Immunol Today 1995, V16, P2 CAPLUS
(4) Caux, C; J Exp Med 1994, V180, P1263 CAPLUS
(5) Caux, C; Res Immunol 1994, V145, P235 CAPLUS
(6) Cella, M; J Exp Med 1996, V184, P747 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

IT **144875-48-9**, R-848
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(dendritic cell maturation and subsequent enhanced T-cell stimulation induced by **immune** response modifier R-848)

L29 ANSWER 14 OF 17 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:555369 CAPLUS
DOCUMENT NUMBER: 132:87525
TITLE: S-28463: treatment of hepatitis C, interferon inducer
AUTHOR(S): Graul, A.; Castaner, J.
CORPORATE SOURCE: Prous Science, Barcelona, 08080, Spain
SOURCE: Drugs Future (1999), 24(6), 622-627
CODEN: DRFUD4; ISSN: 0377-8282
PUBLISHER: Prous Science
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 22 refs. on the synthesis, pharmacol., and clin. studies of S-28463, an interferon inducer with antiviral activity.

REFERENCE COUNT: 26

REFERENCE(S):
(1) Anon; US 5389640 CAPLUS
(2) Anon; WO 9215582 CAPLUS
(3) Anon; WO 9320847 CAPLUS
(8) Fujisawa, H; J Interferon Cytokine Res 1996, V16, P555 CAPLUS
(9) Gerster, J; EP 582581 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

IT **144875-48-9P**, S-28463
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(S-28463: synthesis, antiviral and **immunomodulating** activities)

L29 ANSWER 15 OF 17 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:719269 CAPLUS
DOCUMENT NUMBER: 129:342683
TITLE: Pharmaceutical composition for suppressing type 2 helper T cell immune response
INVENTOR(S): Ochi, Hiroshi; Watanabe, Takamasa; Tomizawa, Hideyuki; Goto, Yuso
PATENT ASSIGNEE(S): Sumitomo Pharmaceuticals Co.,Ltd., Japan; Japan Energy Corp.
SOURCE: PCT Int. Appl., 35 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9848805	A1	19981105	WO 1998-JP1841	19980422

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ,

PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

JP 10298181	A2	19981110	JP 1997-123146	19970425
AU 9870790	A1	19981124	AU 1998-70790	19980422
EP 977569	A1	20000209	EP 1998-917620	19980422

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI

PRIORITY APPLN. INFO.: JP 1997-123146 19970425
WO 1998-JP1841 19980422

OTHER SOURCE(S): MARPAT 129:342683

AB A pharmaceutical compn. for suppressing Th2 type immune response comprises imidazoquinolinamines, specifically 1-(2-methylpropyl)-1H-imidazo[4,5-c]quinolin-4-amine (I), or a pharmaceutically acceptable acid salt thereof, and a method for treating or preventing a disease caused by abnormal activation of Th2 type immune response, such as asthma, allergic dermatitis, allergic rhinitis or systemic lupus erythematosus, which comprises administering a therapeutically effective amt. of the compd. to a patient in need thereof. I strongly suppresses the prodn. of IL-4 and IL-5, and enhances the prodn. of IFN-.gamma. in antigen stimulated lymph node cells. Thus, I has the desired property of suppressing TH2-type immune response and enhancing TH1 type immune response.

IT **99011-02-6**, Imiquimod
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(imidazoquinolinamines for suppressing type 2 helper T cell **immune** response)

L29 ANSWER 16 OF 17 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:394209 CAPLUS
DOCUMENT NUMBER: 129:58813
TITLE: Gel formulations for topical drug delivery
INVENTOR(S): Beaurline, Joseph M.; Roddy, Patrick J.; Tomai, Mark A.
PATENT ASSIGNEE(S): Minnesota Mining and Manufacturing Company, USA
SOURCE: PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9824436	A2	19980611	WO 1997-US21995	19971201

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

AU 9853686	A1	19980629	AU 1998-53686	19971201
AU 723897	B2	20000907		
EP 942724	A2	19990922	EP 1997-950772	19971201

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE, PT, IE

BR 9713677	A	20000328	BR 1997-13677	19971201
JP 2001501968	T2	20010213	JP 1998-525740	19971201
NO 9902638	A	19990716	NO 1999-2638	19990601

PRIORITY APPLN. INFO.: US 1996-759992 A 19961203
WO 1997-US21995 W 19971201

AB Pharmaceutical gel formulations for topical drug delivery include drug, colloidal silicon dioxide, triacetin, and propylene glycol. The gel formulations are well suited for topical delivery of the drug 4-amino-2-ethoxymethyl-.alpha.,.alpha.-dimethyl-1H-imidazo[4,5-c]quinoline-1-ethanol, which when applied topically induces cytokines, such as interferon and tumor necrosis factor, locally in the skin or mucous membranes of a mammal. The gel formulations are also well suited for topical delivery of drugs for treatment of diseases involving skin and/or mucosal lesions because the gel formulations do not need to include

irritating components.

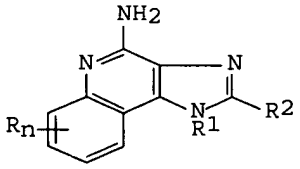
IT **144875-48-9**
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(topical gels contg. imidazoquinolinethanol deriv. for enhancement of immune responses)

L29 ANSWER 17 OF 17 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1988:75403 CAPLUS
DOCUMENT NUMBER: 108:75403
TITLE: Preparation of 1H-imidazo[4,5-c]quinolin-4-amines as antiviral agents and interferon inducers
INVENTOR(S): Gerster, John F.
PATENT ASSIGNEE(S): Riker Laboratories, Inc., USA
SOURCE: U.S., 19 pp. Cont.-in-part of U.S. Ser. No. 553,158, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4689338	A	19870825	US 1985-798385	19851115
IL 84537	A1	19901223	IL 1984-84537	19841116
IL 73534	A1	19901223	IL 1984-73534	19841116
AT 84525	E	19930115	AT 1988-116137	19841116
NO 8900822	A	19850520	NO 1989-822	19890227
NO 165145	B	19900924		
NO 165145	C	19910102		
NO 8900823	A	19850520	NO 1989-823	19890227
NO 165146	B	19900924		
NO 165146	C	19910102		
NO 8900824	A	19850520	NO 1989-824	19890227
NO 165147	B	19900924		
NO 165147	C	19910102		
NO 8900825	A	19850520	NO 1989-825	19890227
NO 169437	B	19920316		
NO 169437	C	19920624		
NO 8900826	A	19850520	NO 1989-826	19890227
NO 168705	B	19911216		
NO 168705	C	19920325		

PRIORITY APPLN. INFO.:
US 1983-553158 19831118
US 1983-553157 19831118
NO 1984-4565 19841115
EP 1988-116137 19841116
IL 1984-73534 19841116

OTHER SOURCE(S): CASREACT 108:75403
GI



I

AB The title compds. [I; R = C1-4 alkyl, C1-4 alkoxy, halo; R1 = C1-10 alkyl, R3OZ, (un)substituted Ph, PhCH2, PhCH2CH2; R2 = H, C1-8 alkyl, (un)substituted Ph, PhCH2, PhCH2CH2; R3 = H, OH, C2-4 alkanoyl, Bz; Z = C1-6 alkylene; n = 1, 2] were prepd. as antiviral agents, esp. against herpes simplex types 1 and 2, and as an interferon inducer. 1-Isobutyl-1H-imidazo[4,5-c]quinoline (prepn. given) was oxidized with H2O2 to give the 5-oxide which was chlorinated with POCl3 and treated with 50% aq. NaOH to give 4-chloro-1-isobutyl-1H-imidazo[4,5-c]quinoline. The

latter was heated at 150.degree. in a bomb with concd. NH4OH to give I (R1 = Me2CHCH2, R = R2 = H) (II). In female guinea pigs 5 mg II/kg intravaginally increased blood interferon activity to 31,250/mL, compared to 100-1000/mL for untreated animals. A topical antiviral cream was prepd. contg. II 1, Me paraben 0.2, Pr paraben 0.02, Avicel CL-611 microcryst. cellulose 5, and H2O 93.78%.

IT 99010-21-6P 99010-30-7P 99010-31-8P 99010-32-9P 99010-42-1P
99010-43-2P 99010-44-3P 99010-45-4P 99010-46-5P 99010-47-6P
99010-55-6P 99010-79-4P 99010-80-7P 99010-82-9P 99010-83-0P
99010-84-1P 99010-85-2P 99010-86-3P 99010-87-4P 99010-88-5P
99010-89-6P 99010-90-9P 99010-91-0P 99010-92-1P 99010-93-2P
99010-94-3P 99010-98-7P 99010-99-8P 99011-00-4P 99011-01-5P
99011-02-6P 99011-03-7P 99011-04-8P 99011-05-9P
99011-06-0P 99011-07-1P 99011-08-2P 99011-09-3P 99011-10-6P
99011-11-7P 99011-12-8P 99011-13-9P 99011-14-0P 99011-15-1P
99011-16-2P 99011-17-3P 99011-18-4P 99011-19-5P 99011-20-8P
99011-21-9P 99011-22-0P 99011-28-6P 99011-65-1P 99011-66-2P
99011-67-3P 99011-68-4P 99011-69-5P 99011-70-8P 99011-71-9P
99011-72-0P 99011-73-1P 99011-74-2P 99011-75-3P 99011-76-4P
99011-77-5P 99011-78-6P 99011-79-7P 99011-80-0P 99011-81-1P
99011-82-2P 99011-85-5P 99023-61-7P 99023-78-6P 99023-79-7P
99023-80-0P 99023-81-1P 99023-82-2P 99023-83-3P 99023-85-5P
99023-87-7P 99023-89-9P 99023-91-3P 99023-93-5P 99023-94-6P
99023-97-9P 99023-98-0P 99023-99-1P 99024-00-7P 99024-01-8P
99024-03-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as virucide and **immunomodulator**)

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=> s corticoster? (s) l11
L33         117 CORTICOSTER? (S) L11

=> dup rem l33
PROCESSING COMPLETED FOR L33
L34          82 DUP REM L33 (35 DUPLICATES REMOVED)

=> d his

     (FILE 'HOME' ENTERED AT 17:06:53 ON 27 DEC 2001)

     FILE 'REGISTRY' ENTERED AT 17:07:01 ON 27 DEC 2001
L1            1 S ZIPRASIDONE/CN

     FILE 'CAPLUS' ENTERED AT 17:07:18 ON 27 DEC 2001

     FILE 'REGISTRY' ENTERED AT 17:07:27 ON 27 DEC 2001
                SEL NAME L1 1

     FILE 'HCAPLUS' ENTERED AT 17:07:50 ON 27 DEC 2001
L2          169 S E1-5 OR L1
L3           93 S L1 AND THU/RL
L4       186327 S ?OBES? OR WEIGHT LOSS OR WEIGHT GAIN OR OVERWEIG?
L5           11 S L3 (S) L4
L6           11 FOCUS L5 1-

     FILE 'REGISTRY' ENTERED AT 17:51:23 ON 27 DEC 2001
L7                STRUCTURE UPLOADED
L8           50 S L7
L9         1291 S L7 FULL

     FILE 'HCAPLUS' ENTERED AT 17:52:23 ON 27 DEC 2001
L10         125 S L9
L11       19621 S ?VENOM?
L12           1 S L10 (S) L11
                SEL RN L12 1

     FILE 'REGISTRY' ENTERED AT 17:53:08 ON 27 DEC 2001
L13           6 S E6-11

     FILE 'CAPLUS' ENTERED AT 17:53:34 ON 27 DEC 2001

     FILE 'MEDLINE, CAPLUS, BIOSIS, USPATFULL' ENTERED AT 17:53:42 ON 27 DEC
     2001
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L14          358 S E6-11
L15          248 DUP REM L14 (110 DUPLICATES REMOVED)
L16      3762735 S ?IMMUN?
L17          182 S L16 AND L15
L18         6743 S L11 (S) L16
L19      8537843 S TREAT? OR THERAP? OR INBIT?
L20        41321 S SPIDER? OR JELLYFISH
L21          215 S L20 (S) L18
L22           51 S L19 (S) L21
L23           51 FOCUS L22 1-

     FILE 'STNGUIDE' ENTERED AT 18:00:02 ON 27 DEC 2001

     FILE 'MEDLINE, CAPLUS, BIOSIS, USPATFULL' ENTERED AT 18:03:14 ON 27 DEC
     2001
L24            1 S L11 (S) L15
L25            1 S L11 AND L15
L26           36 DUP REM L23 (15 DUPLICATES REMOVED)
L27           36 FOCUS L26 1-

     FILE 'STNGUIDE' ENTERED AT 18:08:07 ON 27 DEC 2001

     FILE 'MEDLINE, CAPLUS, BIOSIS, USPATFULL' ENTERED AT 18:08:21 ON 27 DEC
     2001

     FILE 'STNGUIDE' ENTERED AT 18:08:23 ON 27 DEC 2001

     FILE 'MEDLINE, CAPLUS, BIOSIS, USPATFULL' ENTERED AT 18:22:31 ON 27 DEC
     2001

     FILE 'STNGUIDE' ENTERED AT 18:22:45 ON 27 DEC 2001

     FILE 'MEDLINE, CAPLUS, BIOSIS, USPATFULL' ENTERED AT 18:26:40 ON 27 DEC
     2001
L28           17 S L15 (S) IMMUN?
L29           17 FOCUS L28 1-
L30          446 S TH2 MEDIAT?
L31            0 S L30 (S) LL11
L32            0 S L30 (S) LL1
L33          117 S CORTICOSTER? (S) L11
L34           82 DUP REM L33 (35 DUPLICATES REMOVED)

=> s l19 (s) l34
L35          44 L19 (S) L34

=> focus
PROCESSING COMPLETED FOR L35
L36           44 FOCUS L35 1-

=> d ibib abs kwic 1-5

L36  ANSWER 1 OF 44     MEDLINE
ACCESSION NUMBER:    89313407     MEDLINE
DOCUMENT NUMBER:     89313407   PubMed ID: 2664428
TITLE:               Acute arthropod envenomation. Incidence, clinical features
                     and management.
AUTHOR:              Binder L S
CORPORATE SOURCE:    Division of Emergency Medicine, Texas Tech University
                     Regional Academic Health Center, El Paso.
SOURCE:              MEDICAL TOXICOLOGY AND ADVERSE DRUG EXPERIENCE, (1989
                     May-Jun) 4 (3) 163-73.  Ref: 84
                     Journal code: MTD; 8709214. ISSN: 0112-5966.
PUB. COUNTRY:        New Zealand
                     Journal; Article; (JOURNAL ARTICLE)
                     General Review; (REVIEW)
                     (REVIEW, TUTORIAL)
LANGUAGE:            English
FILE SEGMENT:        Priority Journals
ENTRY MONTH:         198908
ENTRY DATE:          Entered STN: 19900309
                     Last Updated on STN: 19900309
                     Entered Medline: 19890825
AB   Black widow spider (Latrodectus mactans) envenomation is found
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throughout both the temperate and tropical latitudes, and is one of the leading causes of death from arthropod **envenomations** worldwide. The **venom** is highly neurotoxic, affecting the presynaptic motor endplate to allow massive noradrenaline (norepinephrine) and acetylcholine release into synapses causing excessive stimulation and fatigue of the motor end plate and muscle. Clinically, patients develop a bite site lesion and pain, abdominal pain and tenderness, and lower extremity pain and weakness within minutes to hours of **envenomation**. Symptoms progress over several hours, then subside over 2 to 3 days. The recommended **treatment** of 'common' **envenomation** is calcium gluconate 10% intravenously, titrated to relief of symptoms; antivenin, although effective, may cause hypersensitivity and serum sickness reactions, and should be restricted to life-threatening **envenomations** only. Brown recluse spider (Loxosceles reclusa) **envenomations** are seen in the Americas and in Europe, and are endemic to the south and central United States. The **venom** contains at least 8 enzymes, consisting of various lysins (facilitating **venom** spread) and sphingomyelinase D, which causes cell membrane injury and lysis, thrombosis, local ischaemia, and chemotaxis. Local **envenomations** begin as pain and itching that progresses to vesiculation with violaceous necrosis and surrounding erythema, and ultimately ulcer formation. Systemic **envenomations** may be life threatening, and present with fever, constitutional symptoms, petechial eruptions, thrombocytopenia, and haemolysis with haemoglobinuric renal failure. **Treatment** of local **envenomations** is conservative (local wound care, cryotherapy, elevation, tetanus prophylaxis, and close follow-up); systemic **envenomation** requires supportive care and **treatment** of arising complications, **corticosteroids** to stabilise red blood cell membranes, and support of renal function. Dapsone 100mg daily has emerged as a promising **therapeutic** agent in both animal studies and clinical trials. Over 650 species of scorpions are known to cause **envenomation** (mostly in children under 10 years); they are endemic mostly in arid and tropical areas. Different **venoms** and clinical presentations are seen across the different species. Most commonly, an inflammatory local reaction occurs with **envenomation**, which is **treated** with wound debridement and cleaning, tetanus prophylaxis, and antihistamines. Occasionally the **venom** is allergenic, and the resultant allergic reaction is **treated** in a standard fashion.(ABSTRACT TRUNCATED AT 400 WORDS)

L36 ANSWER 2 OF 44 MEDLINE
ACCESSION NUMBER: 88009762 MEDLINE
DOCUMENT NUMBER: 88009762 PubMed ID: 3655676
TITLE: Venomous snakebites in the United States.
AUTHOR: Kurecki B A 3rd; Brownlee H J Jr
CORPORATE SOURCE: Family Practice Residency Program, Bayfront Medical Center, St. Petersburg, Florida.
SOURCE: JOURNAL OF FAMILY PRACTICE, (1987 Oct) 25 (4) 386-92.
Journal code: I4L; 7502590. ISSN: 0094-3509.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 198711
ENTRY DATE: Entered STN: 19900305
Last Updated on STN: 19900305
Entered Medline: 19871120

AB **Venomous** snakebite **treatment** is controversial. **Venomous** snakebites are known to occur in all but a few states. Approximately 10 to 15 individuals die from snakebites each year, with bites from diamondback rattlesnakes accounting for 95 percent of fatalities. The identification of the two endogenous classes of **venomous** snakes are discussed in detail to aid in determining the proper **treatment** for each class. Approximately 25 percent of all pit viper bites are "dry" and result in no **envenomation**. The best first aid is a set of car keys to get the victim to a facility where antivenin is obtainable. Incision and suction should be limited to very special situations; cryotherapy and use of tourniquets applied by laymen should be avoided. Proper medical management at a health care facility requires establishing whether **envenomation** has occurred and to what extent, followed by appropriate dosing of antivenin. The use of **corticosteroids** and antibiotics is controversial. Tetanus

immunization should be updated, if necessary. Although research in developing a more purified antivenin is under way, the best **treatment** for snakebite is prevention.

L36 ANSWER 3 OF 44 MEDLINE
ACCESSION NUMBER: 79035573 MEDLINE
DOCUMENT NUMBER: 79035573 PubMed ID: 705419
TITLE: Clinical observations on glucocorticoids in cobra envenomation.
AUTHOR: Mukda Trishnananda; Sararat Yongchaiyudha; Vimala Chayodom
SOURCE: SOUTHEAST ASIAN JOURNAL OF TROPICAL MEDICINE AND PUBLIC HEALTH, (1978 Mar) 9 (1) 71-3.
Journal code: UVN; 0266303. ISSN: 0038-3619.
PUB. COUNTRY: Thailand
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 197812
ENTRY DATE: Entered STN: 19900314
Last Updated on STN: 19900314
Entered Medline: 19781220
AB A clinical trial of **corticosteroid treatment** in five cases of cobra, Naja naja, bite with systemic poisoning is reported. The results reveal that **corticosteroid** had no demonstrable beneficial effect in the neurotoxic poisoning of the cobra. Specific **antivenom** is the most important **therapeutic** agent for systemic poisoning. The combination of **antivenom** and **corticosteroid** had no effect on the development of local necrosis.

L36 ANSWER 4 OF 44 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1979:158353 BIOSIS
DOCUMENT NUMBER: BA67:38353
TITLE: CLINICAL OBSERVATIONS ON GLUCO CORTICOIDS IN COBRA ENVENOMATION.
AUTHOR(S): TRISHNANANDA M; YONGCHAIYUDHA S; CHAYODOM V
CORPORATE SOURCE: DEP. PREV. SOC. MED., FAC. MED., SIRIRAJ HOSP., BANGKOK, THAIL.
SOURCE: SOUTHEAST ASIAN J TROP MED PUBLIC HEALTH, (1978) 9 (1), 71-73.
CODEN: SJTMAK. ISSN: 0125-1562.
FILE SEGMENT: BA; OLD
LANGUAGE: English
AB A clinical trial of **corticosteroid treatment** in 5 cases of cobra, Naja naja, bite with systemic poisoning is reported. The **corticosteroid** had no demonstrable beneficial effect in the neurotoxic poisoning of the cobra. Specific **antivenom** is the most important **therapeutic** agent for systemic poisoning. The combination of **antivenom** and **corticosteroid** had no effect on the development of local necrosis.

L36 ANSWER 5 OF 44 MEDLINE
ACCESSION NUMBER: 68085280 MEDLINE
DOCUMENT NUMBER: 68085280 PubMed ID: 5987628
TITLE: [**Corticosteroid therapy** after poisoning by snake **venoms**, with some observations on the **treatment** of Bothrops nasutus bites].
Die Corticosteroidtherapie nach Intoxikation mit Schlangengiften, sowie eigene Beobachtungen bei der Behandlung eines Bisses von Bothrops nasutus.
AUTHOR: Haas J
SOURCE: ZEITSCHRIFT FUR TROPENMEDIZIN UND PARASITOLOGIE, (1966 Apr) 17 (1) 26-35.
Journal code: Y12; 0423231. ISSN: 0044-359X.
PUB. COUNTRY: GERMANY, WEST: Germany, Federal Republic of
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: German
FILE SEGMENT: Priority Journals
ENTRY MONTH: 196802
ENTRY DATE: Entered STN: 19900101
Last Updated on STN: 19900101
Entered Medline: 19680210
TI [**Corticosteroid therapy** after poisoning by snake **venoms**, with some observations on the **treatment** of

Bothrops nasutus bites].
Die Corticosteroidtherapie nach Intoxikation mit Schlangengiften, sowie eigene Beobachtungen bei der Behandlung eines Bisses von Bothrops. . .

=> d ibib abs kwic 6-10

L36 ANSWER 6 OF 44 MEDLINE
ACCESSION NUMBER: 2000004520 MEDLINE
DOCUMENT NUMBER: 20004520 PubMed ID: 10533009
TITLE: Incidence of immediate and delayed hypersensitivity to Centruroides antivenom.
COMMENT: Comment in: Ann Emerg Med. 1999 Nov;34(5):669-70
AUTHOR: LoVecchio F; Welch S; Klemens J; Curry S C; Thomas R
CORPORATE SOURCE: Department of Medical Toxicology, Good Samaritan Medical Center, Phoenix, AZ 85006, USA.. frankl@samaritan.edu
SOURCE: ANNALS OF EMERGENCY MEDICINE, (1999 Nov) 34 (5) 615-9.
Journal code: 4Z7; 8002646. ISSN: 0196-0644.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199911
ENTRY DATE: Entered STN: 20000111
Last Updated on STN: 20000111
Entered Medline: 19991116
AB STUDY OBJECTIVE: To assess the incidence and course of immediate and delayed hypersensitivity to Centruroides **antivenom**. METHODS: We performed a 12-month prospective observation study, with telephone follow-up, evaluating the incidence of anaphylaxis or anaphylactoid reactions and serum sickness after Centruroides **antivenom** administration. The setting for the study was a poison control center and tertiary care toxicology **treatment** center. Participants included all patients who received Centruroides **antivenom**, and no interventions were performed. RESULTS: For immediate hypersensitivity reactions, 116 patients with grade III or IV **envenomation** received Centruroides **antivenom**; 77 of these patients were younger than 13 years. Three patients completed the infusion despite development of rash. A fourth patient with a history of atopy and asthma received epinephrine infusion and an inhaled beta-agonist for transient wheezing that quickly resolved; she was admitted for observation. Nine patients without hypersensitivity reactions were admitted for social reasons, for inappropriate sedation from drugs used before **antivenom**, or to rule out aspiration; all were discharged within 24 hours. The remaining 106 patients were discharged from the emergency department after resolution of symptoms. Thus 4 of 116 patients had immediate reactions. For patients with delayed reactions, 17 patients were lost to follow-up. Of 99 remaining patients, serum sickness developed in 61% (n=60), as defined by using liberal criteria. Serum sickness responded to oral steroids, antihistamines, or both; mean duration of symptoms with medication was 2.8 days. CONCLUSION: Anaphylactic reactions are uncommon after Centruroides **antivenom** infusion. Self-limited serum sickness that is easily controlled with **corticosteroids** and antihistamines commonly follows the use of Centruroides **antivenom**
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L36 ANSWER 7 OF 44 MEDLINE
ACCESSION NUMBER: 1999216804 MEDLINE
DOCUMENT NUMBER: 99216804 PubMed ID: 10200797
TITLE: Bee sting envenomation resulting in secondary immune-mediated hemolytic anemia in two dogs.
AUTHOR: Noble S J; Armstrong P J
CORPORATE SOURCE: Department of Small Animal Clinical Sciences, College of Veterinary Medicine, University of Minnesota, St Paul 55108, USA.
SOURCE: JOURNAL OF THE AMERICAN VETERINARY MEDICAL ASSOCIATION, (1999 Apr 1) 214 (7) 1026-7, 1021.
Journal code: HAV; 7503067. ISSN: 0003-1488.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals

ENTRY MONTH: 199906
ENTRY DATE: Entered STN: 19990614
Last Updated on STN: 19990614
Entered Medline: 19990603

AB Immune-mediated hemolytic anemia secondary to bee **envenomation** developed in 2 dogs. Clinical signs included lethargy, hematuria, ataxia, and seizures; 1 dog died. Clinicopathologic data included nonregenerative anemia, spherocytosis, positive results for Coombs' test, and occult hematuria. **Treatment** included oral administration of **corticosteroids** at immunosuppressive dosages and supportive care. The surviving dog initially responded to **corticosteroids**, but hemolysis recurred as the dosage was tapered. Hemolysis resolved with prolonged administration of **corticosteroids**. Bee **venom** contains hyaluronidase, histamines, and hemolysins that cause toxic and hemolytic effects. **Envenomation** should be considered in any dog with hemolytic anemia in which other causes are ruled out and exposure to bees is known.

L36 ANSWER 8 OF 44 MEDLINE
ACCESSION NUMBER: 86254387 MEDLINE
DOCUMENT NUMBER: 86254387 PubMed ID: 3723645
TITLE: Ocular effects of the venom from the spitting cobra (Naja nigricollis).
AUTHOR: Ismail M; Ellison A C
SOURCE: JOURNAL OF TOXICOLOGY. CLINICAL TOXICOLOGY, (1986) 24 (3) 183-202.
Journal code: KAN; 8213460. ISSN: 0731-3810.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 198608
ENTRY DATE: Entered STN: 19900321
Last Updated on STN: 19900321
Entered Medline: 19860821

AB N. nigricollis **venom** caused transient corneal oedema, extensive chemosis and pupillary dilation when applied topically to the corneas of albino and pigmented rabbits. After 1 month, permanent corneal scarring, neovascularization and deepithelialization was noted in albino eyes, whereas minimal scarring or deepithelialization occurred in pigmented eyes. In contrast, mydriasis and cycloplegia occurred initially in the pigmented eye, with the pupil remaining fixed and dilated for more than 7 days. The albino pupil, however, returned to normal within 2-3 days. Preliminary penetration studies using labelled **venom** revealed that N. nigricollis **venom** was mainly bound in the corneal stroma of the albino eye and showed poor penetration, whereas minimal corneal binding and poor penetration was noted in the pigmented eye. It appears that the high initial corneal edema may result from the intrinsic release of histamine and acetylcholine. The progression of corneal edema to liquefaction and opacification is probably due to the release of an endogenous corneal damaging factor by the **venom** presumably a collagenase or proteinase. **Treatment** with **corticosteroids** significantly increased the severity of the keratoconjunctivitis and deepithelialization, whereas **treatment** with heparin significantly reduced the keratoconjunctivitis and prevented further opacification. It is postulated that heparin might act through its chelating effect on ions necessary for the action of the proteolytic enzymes.

L36 ANSWER 9 OF 44 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1969:401771 CAPLUS
DOCUMENT NUMBER: 71:1771
TITLE: Effects of adrenalectomy on the changes in cholesterol levels in rats induced by Walterinnesia venom
AUTHOR(S): Zaki, Omer A.; Long, Cyril
CORPORATE SOURCE: Fac. Med., Univ. Khartoum, Khartoum, Sudan
SOURCE: Toxicon (1969), 6(4), 255-61
CODEN: TOXIA6
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In normal rats, the total cholesterol (I) level consisted of 52 mg. of I ester and 34 mg. of free I per 100 ml. of plasma. In the adrenal gland, there was 2.97 mg. of I ester and 1.06 mg. of free I/100 mg. of adrenal

tissue. An i.p. injection of 0.02 mg. of black snake (W. aegyptia) venom decreased the concns. to 39.0 mg. I ester and 27.6 mg. free I/100 ml. plasma, with 0.92 mg. and 0.52 mg./100 mg. adrenal tissue, resp. In untreated adrenalectomized rats, total plasma I was the same as intact animals, but there was an increase of free I and a decrease in I ester. Injection of the sublethal dose of venom into the adrenalectomized animals increased the total plasma I level to 115 mg./100 ml., with 49 mg. as the I ester and 66 mg. as a free I/100 ml. An i.m. injection of 3 mg. **corticosterone**/100 g. abolished the changes in the plasma levels of both free I and I ester caused by **treatment** with the **venom**. When the venom was diluted with plasma over the range 1:640-1:10, hemolysis increased from 6.4 to 100%, with a concurrent increase of I in the suspending fluid, together with a decrease in the erythrocyte I. No hemolysis was detected when the venom was incubated with the erythrocytes in the absence of plasma, and there was change in the erythrocyte I.

L36 ANSWER 10 OF 44 MEDLINE
ACCESSION NUMBER: 2001496612 IN-PROCESS
DOCUMENT NUMBER: 21427974 PubMed ID: 11545249
TITLE: Role of crotoxin, a phospholipase A2 isolated from Crotalus durissus terrificus snake venom, on inflammatory and immune reactions.
AUTHOR: Cardoso D F; Lopes-Ferreira M; Faquim-Mauro E L; Macedo M S; Farsky S H
CORPORATE SOURCE: Laboratory of Immunopathology, Institute Butantan, Sao Paulo, Brazil.
SOURCE: MEDIATORS OF INFLAMMATION, (2001 Jun) 10 (3) 125-33. Journal code: C2M; 9209001. ISSN: 0962-9351.
PUB. COUNTRY: England: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE: Entered STN: 20010910
Last Updated on STN: 20010910

AB BACKGROUND: Crotoxin (CTX) is a potent neurotoxin from Crotalus durissus terrificus snake **venom** (CdtV) composed of two subunits: one without catalytic activity (crotapotin), and a basic phospolipase A2. Recent data have demonstrated that CdtV or CTX inhibit some immune and inflammatory reactions. AIM: The aim of this paper was to investigate the mechanisms involved in these impaired responses. MATERIALS AND METHODS: Male Swiss mice were bled before and at different intervals of time after subcutaneous injection of CTX or bovine serum albumin (BSA) (control animals). The effect of **treatments** on circulating leukocyte mobilisation and on serum levels of interleukin (IL)-6, IL-10, interferon (IFN)-gamma and **corticosterone** were investigated. Spleen cells from **treated** animals were also stimulated in vitro with concanavalin A to evaluate the profile of IL-4, IL-6, IL-10 or IFN-gamma secretion. Cytokine levels were determined by immunoenzymatic assay and **corticosterone** levels by radioimmunoassay. To investigate the participation of endogenous **corticosteroid** on the effects evoked by CTX, animals were **treated** with metyrapone, an inhibitor of glucocorticoid synthesis, previous to CTX **treatment**. RESULTS: Marked alterations on peripheral leukocyte distribution, characterised by a drop in the number of lymphocytes and monocytes and an increase in the number of neutrophils, were observed after CTX injection. No such alteration was observed in BSA-**treated** animals. Increased levels of IL-6, IL-10 and **corticosterone** were also detected in CTX-injected animals. IFN-gamma levels were not modified after **treatments**. In contrast, spleen cells obtained from CTX-**treated** animals and stimulated with concanavalin A secreted less IL-10 and IL-4 in comparison with cells obtained from control animals. Metyrapone pretreatment was effective only to reverse the neutrophilia observed after CTX administration. CONCLUSIONS: Our results suggest that CTX may contribute to the deficient inflammatory and immune responses induced by crude CdtV. CTX induces endogenous mechanisms that are responsible, at least in part, for these impaired responses.

=> d ibib abs kwic 11-15

L36 ANSWER 11 OF 44 MEDLINE
ACCESSION NUMBER: 95024584 MEDLINE

DOCUMENT NUMBER: 95024584 PubMed ID: 7938407
TITLE: Severe and fatal mass attacks by 'killer' bees (Africanized honey bees--Apis mellifera scutellata) in Brazil: clinicopathological studies with measurement of serum venom concentrations.
AUTHOR: Franca F O; Benvenuti L A; Fan H W; Dos Santos D R; Hain S H; Picchi-Martins F R; Cardoso J L; Kamiguti A S; Theakston R D; Warrell D A
CORPORATE SOURCE: Hospital Vital Brazil, Instituto Butantan, Sao Paulo.
SOURCE: QUARTERLY JOURNAL OF MEDICINE, (1994 May) 87 (5) 269-82.
Journal code: QKZ; 0401027. ISSN: 0033-5622.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199411
ENTRY DATE: Entered STN: 19941222
Last Updated on STN: 19941222
Entered Medline: 19941110

AB In Sao Paulo State, Brazil, five males, aged between 8 and 64 years, were attacked by 'Africanized' honey bees (Apis mellifera scutellata). The estimated number of stings received by each patient ranged from > 200 to > 1000. All five were transferred to intensive care units in Sao Paulo City. Clinical features included intravascular haemolysis, respiratory distress with ARDS, hepatic dysfunction, rhabdomyolysis (with myoglobinaemia and myoglobinuria), hypertension and myocardial damage (perhaps explained by release of endogenous catecholamines by **venom** phospholipase A2 and mellitin), shock, coma, acute renal failure and bleeding. Laboratory findings included gross neutrophil leucocytosis, elevated serum enzymes [AST, ALT, LDH, CPK (predominantly CPK-MM)] and creatinine. Clotting times were slightly prolonged. Despite **treatment** with antihistamines, **corticosteroids**, bronchodilators, vasodilators, bicarbonate, mannitol and mechanical ventilation, three of the patients died between 22 and 71 h after the attacks, with histopathological features of ARDS, hepatocellular necrosis, acute tubular necrosis, focal subendocardial necrosis and disseminated intravascular coagulation. Whole bee **venom** and phospholipase A2 (PLA2) antigen concentrations were measured in serum and urine for the first time, using enzyme immunoassay. High **venom** and PLA2 concentrations were detected in serum and urine for more than 50 h after the stings in two fatal cases, in one of which the total circulating unbound whole **venom** was estimated at 27 mg, one hour after the attack. An **antivenom** should be developed to **treat** the increasing numbers of victims of mass attacks by Africanized 'killer' bees in USA, Middle and South America.

L36 ANSWER 12 OF 44 MEDLINE
ACCESSION NUMBER: 88116573 MEDLINE
DOCUMENT NUMBER: 88116573 PubMed ID: 2892880
TITLE: Erythema nodosum following a jellyfish sting.
AUTHOR: Auerbach P S; Hays J T
CORPORATE SOURCE: Vanderbilt University Hospital, Nashville, Tennessee.
SOURCE: JOURNAL OF EMERGENCY MEDICINE, (1987 Nov-Dec) 5 (6) 487-91.
Journal code: IBO; 8412174. ISSN: 0736-4679.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198803
ENTRY DATE: Entered STN: 19900308
Last Updated on STN: 19950206
Entered Medline: 19880318

AB At least 100 of the approximately 9,000 species of coelenterates are dangerous to humans. The most common syndrome following an **envenomation** is an immediate intense dermatitis, with characteristic skin discoloration, local pain, and systemic symptoms. In this case report, we describe a case of erythema nodosum with articular manifestations following **envenomation** with an unknown jellyfish. Serological testing of the victim revealed marked elevation of immunoglobulins G and M directed against Physalia physalis, the Portuguese man-of-war. The patient's condition did not respond to conventional topical **therapy** for coelenterate **envenomation**, but was successfully managed with systemic **corticosteroid** **therapy**. This case demonstrates that the emergency physician

should consider a delayed reaction to a marine **envenomation** in any victim who presents with an acute dermatological disease following immersion in marine coastal waters.

L36 ANSWER 13 OF 44 MEDLINE
ACCESSION NUMBER: 80169310 MEDLINE
DOCUMENT NUMBER: 80169310 PubMed ID: 7368013
TITLE: Boomslang (Dispholidus typus) bite. A case report and a review of diagnosis and management.
AUTHOR: du Toit D M
SOURCE: SOUTH AFRICAN MEDICAL JOURNAL, (1980 Mar 29) 57 (13) 507-10.
Journal code: U4R; 0404520. ISSN: 0038-2469.
PUB. COUNTRY: South Africa
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198006
ENTRY DATE: Entered STN: 19900315
Last Updated on STN: 19900315
Entered Medline: 19800627

AB Very few cases of boomslang (Dispholidus typus) **envenomation** have been described. A case report is presented, illustrating many pitfalls in diagnosis and **treatment**. Despite a fully established clinical picture of diffuse intravascular clotting (DIC), response to specific boomsland **antivenom** was immediate, even as late as 86 hours after the bite. Some of the literature regarding the snake, the clinico-pathological effects of the **venom**, and **treatment** is reviewed and discussed. Administration of specific **antivenom** is the only curative measure, while administration of fresh blood and plasma appears to be the most useful supportive measure. Other measures, including the controversial use of heparin and **corticosteroids**, are discussed. Reactions to the **antivenom**, both early and late, are discussed, and methods of prevention and control of reactions are suggested.

L36 ANSWER 14 OF 44 MEDLINE
ACCESSION NUMBER: 95086214 MEDLINE
DOCUMENT NUMBER: 95086214 PubMed ID: 7994034
TITLE: Prevalence and clinical significance of elevated antiphospholipid antibodies in patients with idiopathic thrombocytopenic purpura.
AUTHOR: Stasi R; Stipa E; Masi M; Oliva F; Sciarra A; Perrotti A; Olivieri M; Zaccari G; Gandolfo G M; Galli M; +
CORPORATE SOURCE: Department of Hematology, University of Rome Tor Vergata, S. Eugenio Hospital, Italy.
SOURCE: BLOOD, (1994 Dec 15) 84 (12) 4203-8.
Journal code: A8G; 7603509. ISSN: 0006-4971.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199501
ENTRY DATE: Entered STN: 19950126
Last Updated on STN: 19950126
Entered Medline: 19950117

AB Antibodies against phospholipid antigens (APA) have been demonstrated in idiopathic thrombocytopenic purpura (ITP), but their clinical and pathogenetic significance has remained elusive. In this study we analyzed the prevalence and clinical features of ITP patients with elevated APA. In addition, we prospectively evaluated APA levels after **treatment** with **corticosteroids** and compared them with platelet-associated immunoglobulin (PAIgG) titers. We studied 149 patients with newly diagnosed ITP. Of these, 78 had a platelet count less than 50 x 10(9)/L and received an initial **treatment** with oral prednisone (PDN). In 71 asymptomatic cases with platelet counts between 50 x 10(9)/L and 120 x 10(9)/L, no **therapy** was scheduled. However, in five of them, the platelet count fell below 50 x 10(9)/L after more than 12 months; these patients were **treated** with PDN. Tests for APA included the measurement of anticardiolipin antibodies (ACA) with a solid-phase immunoassay and the detection of the lupus-like anticoagulant (LA) activity with coagulation tests that included kaolin-clotting time, dilute Russel's Viper **venom** time, activated partial thromboplastin time

(aPTT), and dilute aPTT. Controls consisted of 174 apparently healthy subjects. Either LA or elevated ACA was seen in 69 patients (46.3%) at diagnosis. LA and ACA were both elevated in 24 cases (16.1% of the overall patient population and 34.8% of patients with high APA concentrations). No correlation was found between LA ratio values and ACA-IgG or -IgM titers, or between ACA-IgG and ACA-IgM levels. The presence of these antibodies was not associated with sex, age, platelet count, or the severity of hemorrhages. PAIgG was detected in 106 of 127 cases (83%). Again, no relationship was observed with clinical parameters or with APA levels. However, all cases with elevated APA also had increased PAIgG. With regard to the clinical course, we were not able to detect any significant difference between patients with normal and elevated APA. An initial complete response to prednisone **treatment** was observed in 43 of 83 cases (51.8%), with 13 (15.7%) achieving a prolonged complete remission. APA levels were not significantly modified after PDN **therapy** and on relapse. We conclude that APA positivity is a common finding in patients with ITP and does not select a category with different clinical features. APA levels are not influenced by immunosuppressive **therapy** with steroids and are not related to the activity of the disease. Therefore, we do not support a role for APA in the pathogenesis of ITP.

L36 ANSWER 15 OF 44 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1993:395580 BIOSIS
DOCUMENT NUMBER: PREV199396070880
TITLE: Envenomation caused by poisonous animals.
AUTHOR(S): Azevedo-Marques, Marisa M. De (1); Cupo, Palmira; Hering, Sylvia Evelyn
CORPORATE SOURCE: (1) Dep. Clinica Medica Faculdade Med. Ribeirao Preto-USP
SOURCE: Medicina (Ribeirao Preto), (1992) Vol. 25, No. 4, pp. 539-554.
ISSN: 0076-6046.
DOCUMENT TYPE: Article
LANGUAGE: Portuguese
SUMMARY LANGUAGE: Portuguese; English
AB Pathophysiological, clinical and **therapeutical** aspects of **envenomation** caused by most common poisonous animals in Southwest of Brazil are described. **Envenomation** caused by snakes of genera Bothrops, crotalus or Micrurus, by spiders of genera Loxosceles and Phoneutria and by scorpions of genera Tityus are discussed. When indicated, **antivenom** serotherapy must be given by intravenous route, without dilution, drop by drop and preceded by anti-histamine (H-1 - and H-2 - antagonists) as well **corticosteroids** in order to prevent or reduce hypersensitivity reactions, without needing of skin tests.

=> d ibib abs kwic 16-20

L36 ANSWER 16 OF 44 MEDLINE
ACCESSION NUMBER: 91033392 MEDLINE
DOCUMENT NUMBER: 91033392 PubMed ID: 2227687
TITLE: Brown spider bite.
AUTHOR: Bitterman-Deutsch O; Bergman R; Friedman-Birnbaum R
CORPORATE SOURCE: Dept. of Dermatology, Rambam Medical Center, Haifa.
SOURCE: HAREFUAH, (1990 Sep) 119 (5-6) 137-9.
Journal code: FZF; 0034351. ISSN: 0017-7768.
PUB. COUNTRY: Israel
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Hebrew
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199012
ENTRY DATE: Entered STN: 19910208
Last Updated on STN: 19910208
Entered Medline: 19901219
AB The diagnosis of bite by the brown recluse spider, Loxosceles reclusus, is rarely based on absolute identification of the insect because the victims are usually bitten while sleeping or dressing. More often, the history, clinical findings and course of the bite lead to the diagnosis. For early confirmation up to 24 hours after the bite, the passive hemagglutination test can be used. For older lesions, the in-vitro lymphocyte transformation test is useful, but is available in only a few medical centers. **Treatment** of the bite of the brown recluse spider varies from conservative to more active approaches. Resting, local

cooling, systemic antibiotics to prevent infection and mild anti-inflammatory drugs may be given. In the more active approach oral **corticosteroids** are added in the first 72 hours to the antibiotics, especially in massive bites with necrotic centers greater than 2 cm in diameter, or when there is systemic loxoscelism. Recently, good results have been reported with Avlosulfon (dapsone), which is claimed to cure necrotic cutaneous ulcerations, presumably by reducing the activity of polymorphonuclear leukocytes. Other **treatments** include specific antivenin, (of limited use because it must be administered shortly after the bite), and surgery to prevent spreading of the **venom**. We describe 3 cases of brown spider bite with typical clinical presentations in adults aged 20-40 years. 2 were **treated** with **corticosteroids** and antibiotics and 1 with Avlosulfon and prednisone, all within 72 hours of the bite. 2 recovered completely within a few days, but the third **treated** with prednisone and antibiotics, developed an ulcer which healed only after several months of **treatment**.(ABSTRACT TRUNCATED AT 250 WORDS)

L36 ANSWER 17 OF 44 MEDLINE
ACCESSION NUMBER: 1998374567 MEDLINE
DOCUMENT NUMBER: 98374567 PubMed ID: 9521974
TITLE: Anaphylaxis in children: clinical and allergologic features.
AUTHOR: Novembre E; Cianferoni A; Bernardini R; Mugnaini L; Caffarelli C; Cavagni G; Giovane A; Vierucci A
CORPORATE SOURCE: Allergy and Clinical Immunology Unit, Department of Pediatrics, Florence, Italy.
SOURCE: PEDIATRICS, (1998 Apr) 101 (4) E8.
Journal code: OXV; 0376422. ISSN: 1098-4275.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199809
ENTRY DATE: Entered STN: 19980925
Last Updated on STN: 20010521
Entered Medline: 19980915

AB BACKGROUND: Despite the importance of anaphylaxis, little information is available on its clinical features. OBJECTIVE: To evaluate the clinical and allergologic features of anaphylaxis in children referred to the allergology and immunology unit of A. Meyer Children's Hospital (Florence, Italy) from 1994 to 1996. RESULTS: Ninety-five episodes of anaphylaxis occurred in 76 children (50 boys and 26 girls). Sixty-six children (87%) had only one episode of anaphylaxis, while 10 (13%) had two or more episodes. Sixty-two (82%) of the 76 patients had a personal history of atopic symptoms, although 14 (18%) did not. Sixty (79%) of the 76 children studied had at least one positive skin prick test to one or more of the common inhalant and/or food allergens. Children with **venom** -induced anaphylaxis usually had negative skin tests to the allergens tested. A younger age and eczema were more frequent among children with food-dependent anaphylaxis, whereas an older age together with urticaria-angioedema were common among those with exercise-induced anaphylaxis. The mean latent period (+/-SD) of the anaphylaxis episodes was 15.4 +/- 27.5 minutes. Skin and respiratory manifestations had an earlier onset and were more common than the gastrointestinal and cardiovascular ones. The most frequent clinical manifestation in children with food anaphylaxis was gastrointestinal symptoms, whereas cardiovascular symptoms were rare. The most probable causative agents in the 95 episodes described were foods (57%), drugs (11%), hymenoptera **venom** (12%), exercise (9%), additives (1%), specific immunotherapy (1%), latex (1%), and vaccines (2%), but in 6 cases (6%) the agent was never determined. Among the foods, seafood and milk were the most frequently involved. As for location, 57% of the anaphylactic events occurred in the home (54/95), 12% outdoors (11/95); 5% in restaurants (5/95); 3% in the doctor's office (3/95); 3% in hospitals (3/95); 3% on football fields (3/95); 2% on the beach (2/95); 1% in the gym (1/95); 1% at school (1/95); and 1% in the operating room (1/95). In the remaining 12% of cases (11/95) the site remained unknown. Sixty-two percent of the patients (59/95) were **treated** in an emergency room or hospital, while 32% (30/95) were not (this information is lacking in 6% of the cases [6/95]). Patients were **treated** with **corticosteroids** in 72% of the cases (68/95), with antihistamines in 20% (19/95), with epinephrine in 18% (17/95), with beta2-agonists in 5% (5/95), and with

oxygen in 4% (4/95). CONCLUSIONS: In our area, foods, particularly seafood and milk, seem to be the most important etiologic factors triggering anaphylaxis. Food-induced anaphylaxis often occurs in younger children with a severe food allergy, whereas exercise-induced anaphylaxis occurs more often in older children with a history of urticaria-angioedema. The **venom**-induced variant usually presents itself in nonatopic subjects. Given the fact that most of the children had only one anaphylactic reaction, prevention is almost impossible. Epinephrine, although it is the first-choice **treatment** of anaphylaxis, often goes unused, even in hospitals and doctors' offices.

L36 ANSWER 18 OF 44 MEDLINE
ACCESSION NUMBER: 96431938 MEDLINE
DOCUMENT NUMBER: 96431938 PubMed ID: 8835004
TITLE: [Case report of jellyfish injury].
Fallstudie einer Quallenverletzung.
AUTHOR: Raupp U; Milde P; Goerz G; Plewig G; Burnett J; Heeger T
CORPORATE SOURCE: Hautklinik, Heinrich-Heine-Universitat, Dusseldorf.
SOURCE: HAUTARZT, (1996 Jan) 47 (1) 47-52.
Journal code: G13; 0372755. ISSN: 0017-8470.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: German
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199612
ENTRY DATE: Entered STN: 19970128
Last Updated on STN: 19970128
Entered Medline: 19961204

AB We are presenting a 47-year-old woman who was stung by jellyfish while bathing in the sea of Thailand. Immediately after the injury she developed sharp pain and urticarial erythema of the skin of the knees accompanied by muscle cramps of the entire body. After a few days a toxic contact dermatitis with edematous swelling and ulcerations developed, which did not respond to topical antibiotics or **corticosteroids**. Three weeks later the patient presented with a disseminated urticarial eruption, which at first responded well to topical **treatment** and systemic **corticosteroids**. Over the next few weeks, however, a relapse of the eruption and the ulcerations occurred. Raised titres of IgG and IgM antibodies against different jellyfish from the Indian and Pacific Ocean were detected in the patient's serum by the enzyme-linked immunosorbent assay. Antibodies against bees (class 1) and wasps (class 4) were found by the radioallergosorbent test. The clinical features and the immunological findings led to the diagnosis of toxic and allergic contact dermatitis to jellyfish **venom**. First aid and secondary **treatment** of jellyfish injuries are suggested.

L36 ANSWER 19 OF 44 MEDLINE
ACCESSION NUMBER: 93212250 MEDLINE
DOCUMENT NUMBER: 93212250 PubMed ID: 1844380
TITLE: [Immediate hypersensitivity reactions after intravenous use of antivenin sera: prognostic value of intradermal sensitivity tests].
Reacoes de hipersensibilidade imediatas apos uso intravenoso de soros antivenenos: valor prognostico dos testes de sensibilidade intradermicos.
AUTHOR: Cupo P; Azevedo-Marques M M; de Menezes J B; Hering S E
CORPORATE SOURCE: Departamento de Puericultura e Pediatria, Faculdade de Medicina de Ribeirao Preto, Universidade de Sao Paulo, Brasil.
SOURCE: REVISTA DO INSTITUTO DE MEDICINA TROPICAL DE SAO PAULO, (1991 Mar-Apr) 33 (2) 115-22.
Journal code: S9D; 7507484. ISSN: 0036-4665.
PUB. COUNTRY: Brazil
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Portuguese
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199304
ENTRY DATE: Entered STN: 19930514
Last Updated on STN: 19930514
Entered Medline: 19930429

AB The frequency and class of immediate-type hypersensitivity manifestations were studied in 494 snakebitten and scorpion stung patients who were **treated** with intravenous injections of **antivenom** sera.

These patients were admitted to HC-FMRPUSP from 1983 to 1988. The effectiveness of a hypersensitivity skin test was also investigated. Eighty two out of 320 patients admitted following snake bites (25.6%) had immediate-type reactions consisting of isolated skin lesions (40%), skin lesions plus respiratory manifestations (19%) and gastrointestinal involvement (17%). Anaphylactic shock occurred in ten patients (12%). Thirteen out of 174 patients admitted following scorpion stings had immediate-type reactions (7.5%). There was also a preponderance of skin reactions. Anaphylactic shock was observed in one patient. The positive predictive value of hypersensitivity skin test was 31.8% and its sensibility was 54.8%. These data show that a hypersensitivity skin test is ineffective in predicting immediate-type hypersensitivity manifestations in patients given snake and scorpion **antivenom**. Considering these results, this test should be eliminated as a routine procedure when **treating** victims of poisonous animals. These studies indicate that prior to the administration of **antivenom** anti-histamine (H1- and H2-antagonists) as well **corticosteroids** should be given by i.v. route in order to prevent or reduce hypersensitivity reactions. **Antivenom** sera must always be given under continuous medical surveillance by an intravenous route, without dilution, drop by drop for 15-30 minutes.

L36 ANSWER 20 OF 44 MEDLINE
ACCESSION NUMBER: 92056181 MEDLINE
DOCUMENT NUMBER: 92056181 PubMed ID: 1949333
TITLE: [Allergy to insect stings]. Insektstiksallergi.
AUTHOR: Mosbech H; Dahl R; Malling H J; Pedersen S; Svendsen U G
CORPORATE SOURCE: Medicinsk afdeling TTA, Rigshospitalet, Kobenhavn.
SOURCE: UGESKRIFT FOR LAEGER, (1991 Oct 28) 153 (44) 3067-71. Ref: 30
Journal code: WM8; 0141730. ISSN: 0041-5782.
PUB. COUNTRY: Denmark
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: Danish
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199112
ENTRY DATE: Entered STN: 19920124
Last Updated on STN: 19920124
Entered Medline: 19911219

AB Components in the insect **venom** and probably also in their saliva may have direct toxic effects or may cause sensitization and may result in allergic reactions to subsequent stings. In Denmark, only the stings of honey bees and wasps (yellow jackets) are of clinical significance and it is important to be aware that these insects contain separate allergenic components. Clinical manifestations following stings are observed from all of the organ systems on the whole. The commonest are itching of the skin, urticaria, possibly angioedema and slight generalized symptoms with vertigo, headache and fatigue. Life-threatening reactions may also occur and one or two fatal cases are registered annually in Denmark. It may be difficult to decide whether an allergic or a toxic reaction is involved on the basis of the symptoms. Possible IgE-sensitization must therefore be assessed by means of a prick test and measurement of specific IgE. The main **treatment** in cases of acute systemic reactions is adrenaline which may possibly be supplemented with antihistamine and **corticosteroid**. In cases of massive local reactions and urticaria, antihistamines will, as a rule, prove sufficient. Hyposensitization with insect **venom** preparations eliminates the future risk for systemic insect sting reactions practically entirely and this must be recommended for patients with demonstrated IgE-sensitizing and generalized reactions. At present, **treatment** should be continued for three to five years and protection lasts for a series of years after cessation of **treatment**.

=> s l36 and (spider or jellyfish)
L37 5 L36 AND (SPIDER OR JELLYFISH)

=> d ibib abs kwic tot

L37 ANSWER 1 OF 5 MEDLINE
ACCESSION NUMBER: 96431938 MEDLINE
DOCUMENT NUMBER: 96431938 PubMed ID: 8835004

TITLE: [Case report of **jellyfish** injury].
Fallstudie einer Quallenverletzung.
AUTHOR: Raupp U; Milde P; Goerz G; Plewig G; Burnett J; Heeger T
CORPORATE SOURCE: Hautklinik, Heinrich-Heine-Universitat, Dusseldorf.
SOURCE: HAUTARZT, (1996 Jan) 47 (1) 47-52.
Journal code: G13; 0372755. ISSN: 0017-8470.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: German
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199612
ENTRY DATE: Entered STN: 19970128
Last Updated on STN: 19970128
Entered Medline: 19961204

AB We are presenting a 47-year-old woman who was stung by **jellyfish** while bathing in the sea of Thailand. Immediately after the injury she developed sharp pain and urticarial erythema of the skin of the knees accompanied by muscle cramps of the entire body. After a few days a toxic contact dermatitis with edematous swelling and ulcerations developed, which did not respond to topical antibiotics or **corticosteroids**. Three weeks later the patient presented with a disseminated urticarial eruption, which at first responded well to topical **treatment** and systemic **corticosteroids**. Over the next few weeks, however, a relapse of the eruption and the ulcerations occurred. Raised titres of IgG and IgM antibodies against different **jellyfish** from the Indian and Pacific Ocean were detected in the patient's serum by the enzyme-linked immunosorbent assay. Antibodies against bees (class 1) and wasps (class 4) were found by the radioallergosorbent test. The clinical features and the immunological findings led to the diagnosis of toxic and allergic contact dermatitis to **jellyfish venom**. First aid and secondary **treatment** of **jellyfish** injuries are suggested.

CT . . .
Dermatitis, Allergic Contact: DT, drug therapy
Dermatitis, Allergic Contact: IM, immunology
Enzyme-Linked Immunosorbent Assay
IgG: BL, blood
IgM: BL, blood
***Jellyfish**
Jellyfish: IM, immunology
Middle Age
Radioallergosorbent Test
Skin: IM, immunology
*Skin: IN, injuries

L37 ANSWER 2 OF 5 MEDLINE
ACCESSION NUMBER: 91033392 MEDLINE
DOCUMENT NUMBER: 91033392 PubMed ID: 2227687
TITLE: Brown **spider** bite.
AUTHOR: Bitterman-Deutsch O; Bergman R; Friedman-Birnbaum R
CORPORATE SOURCE: Dept. of Dermatology, Rambam Medical Center, Haifa.
SOURCE: HAREFUAH, (1990 Sep) 119 (5-6) 137-9.
Journal code: FZF; 0034351. ISSN: 0017-7768.
PUB. COUNTRY: Israel
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Hebrew
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199012
ENTRY DATE: Entered STN: 19910208
Last Updated on STN: 19910208
Entered Medline: 19901219

AB The diagnosis of bite by the brown recluse **spider**, Loxosceles reclusus, is rarely based on absolute identification of the insect because the victims are usually bitten while sleeping or dressing. More often, the history, clinical findings and course of the bite lead to the diagnosis. For early confirmation up to 24 hours after the bite, the passive hemagglutination test can be used. For older lesions, the in-vitro lymphocyte transformation test is useful, but is available in only a few medical centers. **Treatment** of the bite of the brown recluse **spider** varies from conservative to more active approaches. Resting, local cooling, systemic antibiotics to prevent infection and mild anti-inflammatory drugs may be given. In the more active approach oral **corticosteroids** are added in the first 72 hours to the

antibiotics, especially in massive bites with necrotic centers greater than 2 cm in diameter, or when there is systemic loxoscelism. Recently, good results have been reported with Avlosulfon (dapsone), which is claimed to cure necrotic cutaneous ulcerations, presumably by reducing the activity of polymorphonuclear leukocytes. Other **treatments** include specific antivenin, (of limited use because it must be administered shortly after the bite), and surgery to prevent spreading of the **venom**. We describe 3 cases of brown **spider** bite with typical clinical presentations in adults aged 20-40 years. 2 were **treated** with **corticosteroids** and antibiotics and 1 with Avlosulfon and prednisone, all within 72 hours of the bite. 2 recovered completely within a few days, but the third **treated** with prednisone and antibiotics, developed an ulcer which healed only after several months of **treatment**.(ABSTRACT TRUNCATED AT 250 WORDS)

L37 ANSWER 3 OF 5 MEDLINE
ACCESSION NUMBER: 89313407 MEDLINE
DOCUMENT NUMBER: 89313407 PubMed ID: 2664428
TITLE: Acute arthropod envenomation. Incidence, clinical features and management.
AUTHOR: Binder L S
CORPORATE SOURCE: Division of Emergency Medicine, Texas Tech University Regional Academic Health Center, El Paso.
SOURCE: MEDICAL TOXICOLOGY AND ADVERSE DRUG EXPERIENCE, (1989 May-Jun) 4 (3) 163-73. Ref: 84
Journal code: MTD; 8709214. ISSN: 0112-5966.
PUB. COUNTRY: New Zealand
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198908
ENTRY DATE: Entered STN: 19900309
Last Updated on STN: 19900309
Entered Medline: 19890825

AB Black widow **spider** (Latrodectus mactans) **envenomation** is found throughout both the temperate and tropical latitudes, and is one of the leading causes of death from arthropod **envenomations** worldwide. The **venom** is highly neurotoxic, affecting the presynaptic motor endplate to allow massive noradrenaline (norepinephrine) and acetylcholine release into synapses causing excessive stimulation and fatigue of the motor end plate and muscle. Clinically, patients develop a bite site lesion and pain, abdominal pain and tenderness, and lower extremity pain and weakness within minutes to hours of **envenomation**. Symptoms progress over several hours, then subside over 2 to 3 days. The recommended **treatment** of 'common' **envenomation** is calcium gluconate 10% intravenously, titrated to relief of symptoms; antivenin, although effective, may cause hypersensitivity and serum sickness reactions, and should be restricted to life-threatening **envenomations** only. Brown recluse **spider** (Loxosceles reclusa) **envenomations** are seen in the Americas and in Europe, and are endemic to the south and central United States. The **venom** contains at least 8 enzymes, consisting of various lysins (facilitating **venom** spread) and sphingomyelinase D, which causes cell membrane injury and lysis, thrombosis, local ischaemia, and chemotaxis. Local **envenomations** begin as pain and itching that progresses to vesiculation with violaceous necrosis and surrounding erythema, and ultimately ulcer formation. Systemic **envenomations** may be life threatening, and present with fever, constitutional symptoms, petechial eruptions, thrombocytopenia, and haemolysis with haemoglobinuric renal failure. **Treatment** of local **envenomations** is conservative (local wound care, cryotherapy, elevation, tetanus prophylaxis, and close follow-up); systemic **envenomation** requires supportive care and **treatment** of arising complications, **corticosteroids** to stabilise red blood cell membranes, and support of renal function. Dapsone 100mg daily has emerged as a promising **therapeutic** agent in both animal studies and clinical trials. Over 650 species of scorpions are known to cause **envenomation** (mostly in children under 10 years); they are endemic mostly in arid and tropical areas. Different **venoms** and clinical presentations are seen across the different species. Most commonly, an inflammatory local reaction occurs with

envenomation, which is **treated** with wound debridement and cleaning, tetanus prophylaxis, and antihistamines. Occasionally the **venom** is allergenic, and the resultant allergic reaction is **treated** in a standard fashion.(ABSTRACT TRUNCATED AT 400 WORDS)

L37 ANSWER 4 OF 5 MEDLINE
ACCESSION NUMBER: 88116573 MEDLINE
DOCUMENT NUMBER: 88116573 PubMed ID: 2892880
TITLE: Erythema nodosum following a **jellyfish** sting.
AUTHOR: Auerbach P S; Hays J T
CORPORATE SOURCE: Vanderbilt University Hospital, Nashville, Tennessee.
SOURCE: JOURNAL OF EMERGENCY MEDICINE, (1987 Nov-Dec) 5 (6) 487-91.
Journal code: IBO; 8412174. ISSN: 0736-4679.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198803
ENTRY DATE: Entered STN: 19900308
Last Updated on STN: 19950206
Entered Medline: 19880318

AB At least 100 of the approximately 9,000 species of coelenterates are dangerous to humans. The most common syndrome following an **envenomation** is an immediate intense dermatitis, with characteristic skin discoloration, local pain, and systemic symptoms. In this case report, we describe a case of erythema nodosum with articular manifestations following **envenomation** with an unknown **jellyfish**. Serological testing of the victim revealed marked elevation of immunoglobulins G and M directed against Physalia physalis, the Portuguese man-of-war. The patient's condition did not respond to conventional topical **therapy** for coelenterate **envenomation**, but was successfully managed with systemic **corticosteroid therapy**. This case demonstrates that the emergency physician should consider a delayed reaction to a marine **envenomation** in any victim who presents with an acute dermatological disease following immersion in marine coastal waters.

*Bites and Stings: CO, complications
*Cnidaria
Cnidaria: IM, immunology
*Emergencies
*Erythema Nodosum: ET, etiology
IgG: AN, analysis
IgM: AN, analysis
***Jellyfish**
Jellyfish: IM, immunology
Middle Age
Synovitis: ET, etiology

L37 ANSWER 5 OF 5 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1993:395580 BIOSIS
DOCUMENT NUMBER: PREV199396070880
TITLE: Envenomation caused by poisonous animals.
AUTHOR(S): Azevedo-Marques, Marisa M. De (1); Cupo, Palmira; Hering, Sylvia Evelyn
CORPORATE SOURCE: (1) Dep. Clinica Medica Faculdade Med. Ribeirao Preto-USP
SOURCE: Medicina (Ribeirao Preto), (1992) Vol. 25, No. 4, pp. 539-554.
ISSN: 0076-6046.
DOCUMENT TYPE: Article
LANGUAGE: Portuguese
SUMMARY LANGUAGE: Portuguese; English

AB Pathophysiological, clinical and **therapeutical** aspects of **envenomation** caused by most common poisonous animals in Southwest of Brazil are described. **Envenomation** caused by snakes of genera Bothrops, crotalus or Micrurus, by **spiders** of genera Loxosceles and Phoneutria and by scorpions of genera Tityus are discussed. When indicated, **antivenom** serotherapy must be given by intravenous route, without dilution, drop by drop and preceded by anti-histamine (H-1 - and H-2 - antagonists) as well **corticosteroids** in order to prevent or reduce hypersensitivity reactions, without needing of skin tests.

=> s hypersensitiv? or l11

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L38     206377 HYPERSENSITIV? OR L11

=> s l38 and (spider or jellyfish)
L39       4366 L38 AND (SPIDER OR JELLYFISH)

=> s T helper
L40      28174 T HELPER

=> s l39 (s) l40
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L135 (S) L140'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L136 (S) L141'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L137 (S) L142'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L138 (S) L143'
L41           9 L39 (S) L40

=> dup rem l41
PROCESSING COMPLETED FOR L41
L42           9 DUP REM L41 (0 DUPLICATES REMOVED)

=> focus
PROCESSING COMPLETED FOR L42
L43           9 FOCUS L42 1-

=> d ibib abs kwic 1-5

L43  ANSWER 1 OF 9  USPATFULL
ACCESSION NUMBER:       1998:98886  USPATFULL
TITLE:                  Ectoparasite saliva proteins and apparatus to collect
                        such proteins
INVENTOR(S):            Frank, Glenn R., Wellington, CO, United States
                        Hunter, Shirley Wu, Ft. Collins, CO, United States
                        Wallenfels, Lynda, Ft. Collins, CO, United States
PATENT ASSIGNEE(S):     Heska Corporation, Ft. Collins, CO, United States (U.S.
                        corporation)

                             NUMBER       KIND    DATE
                        ---------------- ------ --------
PATENT INFORMATION:     US 5795862              19980818
APPLICATION INFO.:      US 1995-487001          19950607  (8)
RELATED APPLN. INFO.:   Continuation-in-part of Ser. No. US 1994-319590, filed
                        on 7 Oct 1994, now patented, Pat. No. US 5646115
DOCUMENT TYPE:          Utility
FILE SEGMENT:           Granted
PRIMARY EXAMINER:       Jacobson, Dian C.
LEGAL REPRESENTATIVE:   Sherifan Ross P.C.
NUMBER OF CLAIMS:       29
EXEMPLARY CLAIM:        1
NUMBER OF DRAWINGS:     12 Drawing Figure(s); 12 Drawing Page(s)
LINE COUNT:             4678
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB      The present invention is directed to a novel product and method for
        isolating ectoparasite saliva proteins, and a novel product and method
        for detecting and/or treating allergic dermatitis in an animal. The
        present invention includes a saliva protein collection apparatus capable
        of collecting ectoparasite saliva proteins substantially free of
        contaminating material. The present invention also relates to
        ectoparasite saliva proteins, nucleic acid molecules having sequences
        that encode such proteins, and antibodies raised against such proteins.
        The present invention also includes methods to obtain such proteins and
        to use such proteins to identify animals susceptible to or having
        allergic dermatitis. The present invention also includes therapeutic
        compositions comprising such proteins and their use to treat animals
        susceptible to or having allergic dermatitis.


L43  ANSWER 2 OF 9  USPATFULL
ACCESSION NUMBER:       1999:83583  USPATFULL
TITLE:                  Ectoparasite saliva proteins and apparatus to collect
                        such proteins
```

INVENTOR(S): Frank, Glenn R., Wellington, CO, United States
Hunter, Shirley Wu, Ft. Collins, CO, United States
Wallenfels, Lynda, Ft. Collins, CO, United States
PATENT ASSIGNEE(S): Heska Corporation, Ft. Collins, CO, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5927230		19990727
APPLICATION INFO.:	US 1996-711905		19960912 (8)

RELATED APPLN. INFO.: Division of Ser. No. US 1994-319590, filed on 7 Oct 1994, now patented, Pat. No. US 5646115
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Price, Thomas
LEGAL REPRESENTATIVE: Sheridan Ross, P.C.
NUMBER OF CLAIMS: 11
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 12 Drawing Figure(s); 12 Drawing Page(s)
LINE COUNT: 3771
AB The present invention is directed to a novel product and method for isolating ectoparasite saliva proteins, and a novel product and method for detecting and/or treating allergic dermatitis in an animal. The present invention includes a saliva protein collection apparatus capable of collecting ectoparasite saliva proteins substantially free of contaminating material. The present invention also relates to ectoparasite saliva proteins, nucleic acid molecules having sequences that encode such proteins, and antibodies raised against such proteins. The present invention also includes methods to obtain such proteins and to use such proteins to identify animals susceptible to or having allergic dermatitis. The present invention also includes therapeutic compositions comprising such proteins and their use to treat animals susceptible to or having allergic dermatitis.

L43 ANSWER 3 OF 9 USPATFULL
ACCESSION NUMBER: 97:59173 USPATFULL
TITLE: Ectoparasite saliva proteins and apparatus to collect such proteins
INVENTOR(S): Frank, Glenn R., Wellington, CO, United States
Hunter, Shirley Wu, Ft. Collins, CO, United States
Wallenfels, Lynda, Ft. Collins, CO, United States
PATENT ASSIGNEE(S): Heska Corporation, Ft. Collins, CO, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5646115		19970708
APPLICATION INFO.:	US 1994-319590		19941007 (8)

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Jacobson, Dian C.
LEGAL REPRESENTATIVE: Sheridan Ross & McIntosh
NUMBER OF CLAIMS: 33
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 12 Drawing Figure(s); 12 Drawing Page(s)
LINE COUNT: 3822
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention is directed to a novel product and method for isolating ectoparasite saliva proteins, and a novel product and method for detecting and/or treating allergic dermatitis in an animal. The present invention includes a saliva protein collection apparatus capable of collecting ectoparasite saliva proteins substantially free of contaminating material. The present invention also relates to ectoparasite saliva proteins, nucleic acid molecules having sequences that encode such proteins, and antibodies raised against such proteins. The present invention also includes methods to obtain such proteins and to use such proteins to identify animals susceptible to or having allergic dermatitis. The present invention also includes therapeutic compositions comprising such proteins and their use to treat animals susceptible to or having allergic dermatitis.

L43 ANSWER 4 OF 9 USPATFULL
ACCESSION NUMBER: 1998:147412 USPATFULL
TITLE: Ectoparasite saliva proteins and apparatus to collect

such proteins

INVENTOR(S): Frank, Glenn R., Wellington, CO, United States
Hunter, Shirley Wu, Ft. Collins, CO, United States
Wallenfels, Lynda, St. George, UT, United States

PATENT ASSIGNEE(S): Heska Corporation, Ft. Collins, CO, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5840695		19981124
APPLICATION INFO.:	US 1996-630822		19960410 (8)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1995-487001, filed on 7 Jun 1995, now patented, Pat. No. US 5795862 which is a continuation-in-part of Ser. No. US 1995-487608, filed on 7 Jun 1995 which is a continuation-in-part of Ser. No. US 1994-319590, filed on 7 Oct 1994, now patented, Pat. No. US 5646115

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Wax, Robert A.
ASSISTANT EXAMINER: Stole, Einar
LEGAL REPRESENTATIVE: Sheridan Ross P.C.
NUMBER OF CLAIMS: 41
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 16 Drawing Figure(s); 16 Drawing Page(s)
LINE COUNT: 6531

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention is directed to a novel product and method for isolating ectoparasite saliva proteins, and a novel product and method for detecting and/or treating allergic dermatitis in an animal. The present invention includes a saliva protein collection apparatus capable of collecting ectoparasite saliva proteins substantially free of contaminating material. The present invention also relates to ectoparasite saliva proteins, nucleic acid molecules having sequences that encode such proteins, and antibodies raised against such proteins. The present invention also includes methods to obtain such proteins and to use such proteins to identify animals susceptible to or having allergic dermatitis. The present invention also includes therapeutic compositions comprising such proteins and their use to treat animals susceptible to or having allergic dermatitis.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM Bites from ectoparasites, in particular fleas, can cause a **hypersensitive** response in animals. In particular, **hypersensitive** responses to fleabites is manifested in a disease called flea allergy dermatitis (FAD). **Hypersensitivity** refers to a state of altered reactivity in which an animal, having been previously exposed to a compound, exhibits an allergic response to the compound upon subsequent exposures. **Hypersensitive** responses include immediate and delayed-type **hypersensitivity**, and in particular Type I, Type II, Type III and Type IV **hypersensitivities** (described in detail in Janeway et al., Immunobiology, Garland Publishing, New York, 1994, which is incorporated in its entirety by. . .

SUMM Foreign compounds that induce symptoms of immediate and/or delayed **hypersensitivity** are herein referred to as allergens. The term "allergen" primarily refers to foreign compounds capable of causing an allergic response.. . . interchangeably with the term "antigen," especially with respect to a foreign compound capable of inducing symptoms of immediate and/or delayed **hypersensitivity**. Factors that influence an animal's susceptibility to an allergen can include a genetic component and/or environmental exposure to an allergen. Animals can be de-sensitized to an allergen by repeated injections of the allergen to which an animal is **hypersensitive**.

SUMM FAD can have manifestations of both immediate and delayed-type **hypersensitivity** (described in detail in Janeway et al., ibid.). Effective treatment of FAD has been difficult if not impossible to achieve.. . .

SUMM Thus, there remains a need to more clearly define flea saliva allergens capable of inducing a **hypersensitive** response in animals. In addition, there remains a need to develop a method to collect substantially pure flea saliva allergens. . .

SUMM . . . is about the same size as the reaction to the negative control

solution. In particular, the method can detect immediate **hypersensitivity** and/or delayed **hypersensitivity**.

SUMM . . . or has allergic dermatitis. In particular, the method can be used to detect IgE antibodies as an indicator of immediate **hypersensitivity** in the animal.

DRWD . . . from the bites of ectoparasites. A preferred ectoparasite saliva protein homologue includes at least one epitope capable of eliciting a **hypersensitive** response to the natural ectoparasite saliva protein counterpart. An ectoparasite saliva protein homologue can also include an epitope capable of. . . ability of an ectoparasite saliva protein homologue to detect and/or treat (i.e., immunomodulate or regulate by, for example, desensitizing) the **hypersensitivity** of an animal susceptible to or having allergic dermatitis, can be tested using techniques known to those skilled in the. . .

DRWD . . . sand flies, black flies, horse flies, horn flies, deer flies, tsetse flies, stable flies, myiasis-causing flies and biting gnats; ants; **spiders**, lice; mites; and true bugs, such as bed bugs and kissing bugs, including those carrying Chagas disease. Even more preferred. . .

DRWD . . . invention can contribute to an epitope's ability to induce an allergic response against the protein in an immediate or delayed **hypersensitivity** response.

DRWD . . . the present invention to carry out its function (e.g., anti-coagulation, anti-complement, vasodialators, proteases, acid phosphatases or detecting and/or treating the **hypersensitivity** of an animal susceptible to or having allergic dermatitis). A mimetope can be a peptide that has been modified to. . .

DRWD One embodiment of the present invention is an in vivo test that is capable of detecting whether an animal is **hypersensitive** to ectoparasite saliva products. An in vivo test of the present invention can initially be used to determine if an animal is **hypersensitive** to ectoparasite saliva products and then used to determine if an animal is **hypersensitive** to a particular ectoparasite saliva component, in particular to an ectoparasite saliva protein. An in vivo **hypersensitivity** test of the present invention is particularly useful for identifying animals susceptible to or having allergic dermatitis. An in vivo **hypersensitivity** test of the present invention is even more useful for identifying animals susceptible to or having FAD. A suitable in vivo **hypersensitivity** test of the present invention can be, but is not limited to, a skin test comprising administering (e.g., intradermally injecting. . .

DRWD . . . novel aspect, however, of the present invention is that an ectoparasite saliva product of the present invention can induce a **hypersensitive** response in the absence of an immunopotentiator.

DRWD . . . positive control solution of the present invention contains an effective amount of at least one compound known to induce a **hypersensitive** response when administered to an animal. A preferred compound for use as positive control solution includes, but is not limited. . . histamine. A negative control solution of the present invention can comprise a solution that is known not to induce a **hypersensitive** response when administered to an animal. As such, a negative control solution can comprise a solution having compounds essentially incapable of inducing a **hypersensitive** response or simply a buffer used to prepare the formulation, such as saline. An example of a preferred negative control. . .

DRWD **Hypersensitivity** of an animal to one or more formulations of the present invention can be evaluated by measuring reactions (e.g., wheal. . . syringes. Preferred devices for scratching include devices that permit the administration of a number of samples at one time. The **hypersensitivity** of an animal can be evaluated by determining if the reaction resulting from administration of a formulation of the present. . . the size of a wheal produced by administration of a positive control sample to an animal, then that animal is **hypersensitive** to the experimental sample. Conversely, if an experimental sample produces a reaction similar to the reaction produced by administration of a negative control sample to an animal, then that animal is not **hypersensitive** to the experimental sample.

DRWD Preferred wheal sizes for evaluation of the **hypersensitivity** of an animal range from about 16 mm to about 8 mm, more preferably from about 15 mm to about. . .

DRWD Preferably, the ability or inability of an animal to exhibit an

immediate **hypersensitive** response to a formulation of the present invention is determined by measuring wheal sizes from about 2 minutes to about. . .

DRWD Preferably, the ability or inability of an animal to exhibit a delayed **hypersensitive** response to a formulation of the present invention is determined by measuring induration and/or erythema from about 18 hours to. . . after administration of a sample, and even more preferably at about 24 hours after administration of a sample. A delayed **hypersensitivity** response can also be measured using other techniques such as by determining, using techniques known to those of skill in. . .

DRWD Animals suitable and preferred to test for **hypersensitivity** to ectoparasite saliva proteins using a skin test of the present invention are disclosed herein. Particularly preferred animals to test. . .

DRWD . . . allergic dermatitis by demonstrating that an animal has been previously exposed to an ectoparasite saliva antigen and, therefore may be **hypersensitive** to further exposure to an ectoparasite saliva antigen.

DRWD According to the present invention, an in vitro **hypersensitivity** test of the present invention can be, but is not limited to, an immunoabsorbent test comprising: (a) contacting a formulation. . . dermatitis. The immunoabsorbent test is particularly useful for the detection of IgE antibodies in the body fluid, thereby indicating immediate **hypersensitivity** in the animal. Determining the amount of immunocomplex formed can include the step of separating depending on the mode of. . .

DRWD . . . capable if being inserted into a test tube. Suitable and preferred flea saliva products for use with an in vitro **hypersensitivity** test of the present invention are as disclosed for a skin test of the present invention.

DRWD A second step of a preferred in vitro **hypersensitivity** test of the present invention comprises contacting the coated substrate with a body fluid, such as serum, plasma or whole. . .

DRWD A third step of a preferred in vitro **hypersensitivity** test of the present invention comprises contacting the immunocomplexes bound to the substrate with a compound capable of binding to. . .

DRWD A fourth step of a preferred in vitro **hypersensitivity** test of the present invention comprises measuring the amount of detectable label bound to the solid substrate using techniques known. . .

DRWD A **hypersensitive** animal is identified by comparing the level of immunocomplex formation using samples of body fluid with the level of immunocomplex. . . or equal to immunocomplex formation using a positive control sample, then the animal from which the fluid was taken is **hypersensitive** to the ectoparasite saliva product bound to the substrate. Conversely, if a body fluid sample results in immunocomplex formation similar to immunocomplex formation using a negative control sample, then the animal from which the fluid was taken is not **hypersensitive** to the ectoparasite saliva product bound to the substrate.

DRWD A preferred embodiment of an in vitro **hypersensitivity** test of the present invention comprises the steps of: (a) contacting an ELISA plate, which is coated with a suitable. . .

DRWD . . . for determining if an animal is susceptible to or has allergic dermatitis can include an in vivo or in vitro **hypersensitivity** test of the present invention as described in detail above. A kit of the present invention further comprises at least. . .

DRWD . . . more different in vivo and/or in vitro tests can be used in combination for diagnostic purposes. For example, the immediate **hypersensitivity** of an animal to an ectoparasite saliva allergen can be tested using an in vitro immunoabsorbent test capable of detecting IgE antibodies specific for an ectoparasite saliva allergen in the animal's bodily fluid. While most animals that display delayed **hypersensitivity** to an ectoparasite saliva allergen also display immediate **hypersensitivity** to the allergen, a small number of animals that display delayed **hypersensitivity** to an allergen do not display immediate **hypersensitivity** to the allergen. In such cases, following negative results from the IgE-specific in vitro test, the delayed **hypersensitivity** of the animal to an ectoparasite saliva allergen can be tested using an in vivo test of the present invention.

DRWD . . . formulation of the present invention. According to the present invention, the term treatment can refer to the regulation of a **hypersensitive** response by an animal to bites from

ectoparasites. Regulation can include, for example, immunomodulation of cells involved in the animal's **hypersensitive** response or alteration of the ability of an ectoparasite to introduce allergens into an animal, for example by inhibiting the. . . particular, immunomodulation refers to modulation of antigen:antibody interactions resulting in inflammatory responses, immunosuppression, and immunotolerization of cells involved in a **hypersensitive** response. Immunosuppression refers to inhibiting an immune response by, for example, killing particular cells involved in the immune response. Immunotolerization. . .

DRWD . . . response of the animal (i.e., immunomodulating the animal) so as to block (i.e., to inhibit, reduce or substantially prevent) a **hypersensitive** response by the animal upon subsequent exposure to allergenic components transmitted through bites from ectoparasites. Such a therapeutic composition is useful for immunomodulating animals known to be **hypersensitive** to ectoparasite saliva products and animals susceptible to **hypersensitive** responses against ectoparasite saliva products.

DRWD . . . membranes, cochleates or micelles. A soluble de-sensitizing compound of the present invention is useful for: (1) inhibiting a Type I **hypersensitivity** reaction by blocking IgE:antigen mediated de-granulation of mast cells; (2) inhibiting a Type III **hypersensitivity** reaction by blocking IgG:antigen complex formation leading to complement destruction of cells; and (3) inhibiting a Type IV **hypersensitivity** reaction by blocking **T helper** cell stimulation of cytokine secretion by macrophages. A membrane-bound de-sensitizing compound of the present invention is useful for: (1) inhibiting a Type II **hypersensitivity** reaction by blocking IgG:antigen complex formation on the surface of cells leading to complement destruction of cells; (2) inhibiting a Type II **hypersensitivity** reaction by blocking IgG regulated signal transduction in immune cells; and (3) inhibiting a Type IV **hypersensitivity** reaction by blocking T cytotoxic cell killing of antigen-bearing cells.

DRWD . . . be covalently linked to a ligand molecule capable of targeting the de-sensitizing compound to a specific cell involved in a **hypersensitive** response to ectoparasite saliva products. Appropriate ligands with which to link a desensitizing compound include, for example, at least a. . .

DRWD . . . accomplished by those skilled in the art. An effective dose refers to a dose capable of treating an animal against **hypersensitivity** to ectoparasite saliva allergens. Effective doses can vary depending upon, for example, the therapeutic composition used, the arthropod from which. . . doses to immunomodulate an animal against ectoparasite saliva allergens include doses administered over time that are capable of alleviating a **hypersensitive** response by an animal to ectoparasite saliva allergens. For example, a first tolerizing dose can comprise an amount of a therapeutic composition of the present invention that causes a minimal **hypersensitive** response when administered to a **hypersensitive** animal. A second tolerizing dose can comprise a greater amount of the same therapeutic composition than the first dose. Effective. . . comprise increasing concentrations of the therapeutic composition necessary to tolerize an animal such that the animal does not have a **hypersensitive** response to the bite of an ectoparasite. An effective dose to desensitize an animal can comprise a concentration of a therapeutic composition of the present invention sufficient to block an animal from having a **hypersensitive** response to the bite of an ectoparasite. Effective desensitizing doses can include repeated doses having concentrations of a therapeutic composition that cause a minimal **hypersensitive** response when administered to a **hypersensitive** animal.

DRWD A suitable single dose is a dose that is capable of treating an animal against **hypersensitivity** to ectoparasite saliva allergens when administered one or more times over a suitable time period. For example, a preferred single. . . the original administration. Further treatments with the therapeutic composition preferably are administered when the animal is no longer protected from **hypersensitive** responses to ectoparasite. Particular administration doses and schedules can be developed by one of skill in the art based upon. . .

DRWD A therapeutic composition of the present invention can be used in conjunction with other compounds capable of modifying an animal's **hypersensitivity** to ectoparasite bites. For example, an animal

can be treated with compounds capable of modifying the function of a cell involved in a **hypersensitive** response, compounds that reduce allergic reactions, such as by systemic agents or anti-inflammatory agents (e.g., anti-histamines, anti-steroid reagents, anti-inflammatory reagents. . . chain class switching from IgE to IgG). Suitable compounds useful for modifying the function of a cell involved in a **hypersensitive** response include, but are not limited to, antihistamines, cromolyn sodium, theophylline, cyclosporin A, adrenalin, cortisone, compounds capable of regulating cellular. . .

DETD . . . products produced as described in Examples 2 and 3 include at least one allergenic protein capable of inducing an immediate **hypersensitive** response in a sensitized dog. In particular, injection of the mixtures of flea saliva antigens referred to as FS-1 and. . .

DETD . . . formulations produced as described in Examples 2 and 3 include at least one allergenic protein capable of inducing a delayed **hypersensitive** response in a sensitized dog. Injection of the mixtures of flea saliva proteins referred to as FS-1 and FS-2 induced. . .

DETD . . . in FIGS. 5 through 9, indicate that saliva protein formulations of the present invention are sufficiently allergenic to induce a **hypersensitive** response in a sensitized dog. Numerous samples induced both an immediate **hypersensitive** response and a delayed **hypersensitive** response.

DETD This example demonstrates the ability of numerous flea saliva protein samples isolated in Examples 2 and 3 to induce a **hypersensitive** response by histopathology of tissue removed from selected lesions on the dogs described in Example 8.

DETD . . . mastocytic and eosinophilic, subacute dermatitis. Lesions noted in all the slide specimens examined are consistent with an allergic Type I **hypersensitivity** reaction.

DETD . . . 10 dogs with non-flea-related pruritic dermatoses including, but not limited to, atopy, food allergy dermatitis, pyoderma, seborrhea, and other parasitic **hypersensitivity** reactions; and (3) 10 dogs with normal skin and no history of chronic skin diseases. The dogs were of any. . .

DETD . . . 2.0 .mu.g E. coli-produced fspN3; (h) 0.2 .mu.g S. frugiperda-produced fspN3; and (i) 2.0 .mu.g S. frugiperda-produced fspN3. The immediate **hypersensitivity** results are shown in Table 20, and the delayed **hypersensitivity** results are shown in Table 21. Scoring was as described in Example 8; NA indicates a bad injection.

DETD . . . also exhibited a positive immediate reaction in 4 and all dogs, respectively. The two dogs that showed a strong delayed **hypersensitive** response reaction to FS-1 showed similar delayed **hypersensitive** response reactions to recombinantly produced fspH and fspN3.

CLM What is claimed is:

. . . formulation of claim 1, wherein said ectoparasite is selected from the group consisting of fleas, flies, mosquitoes, ticks, mites, lice, **spiders**, ants and true bugs.

L43 ANSWER 5 OF 9 USPATFULL

ACCESSION NUMBER: 1999:89047 USPATFULL

TITLE: Ectoparasite saliva proteins and apparatus to collect such proteins

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CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention is directed to a novel product and method for isolating ectoparasite saliva proteins, and a novel product and method for detecting and/or treating allergic dermatitis in an animal. The present invention includes a saliva protein collection apparatus capable of collecting ectoparasite saliva proteins substantially free of contaminating material. The present invention also relates to ectoparasite saliva proteins, nucleic acid molecules having sequences that encode such proteins, and antibodies raised against such proteins. The present invention also includes methods to obtain such proteins and to use such proteins to identify animals susceptible to or having allergic dermatitis. The present invention also includes therapeutic compositions comprising such proteins and their use to treat animals susceptible to or having allergic dermatitis.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM Bites from ectoparasites, in particular fleas, can cause a **hypersensitive** response in animals. In particular, **hypersensitive** responses to fleabites is manifested in a disease called flea allergy dermatitis (FAD). **Hypersensitivity** refers to a state of altered reactivity in which an animal, having been previously exposed to a compound, exhibits an allergic response to the compound upon subsequent exposures. **Hypersensitive** responses include immediate and delayed-type **hypersensitivity**, and in particular Type I, Type II, Type III and Type IV **hypersensitivities** (described in detail in Janeway et al., Immunobiology, Garland Publishing, New York, 1994, which is incorporated in its entirety by. . .

SUMM Foreign compounds that induce symptoms of immediate and/or delayed **hypersensitivity** are herein referred to as allergens. The term "allergen" primarily refers to foreign compounds capable of causing an allergic response.. . . interchangeably with the term "antigen," especially with respect to a foreign compound capable of inducing symptoms of immediate and/or delayed **hypersensitivity**. Factors that influence an animal's susceptibility to an allergen can include a genetic component and/or environmental exposure to an allergen. Animals can be de-sensitized to an allergen by repeated injections of the allergen to which an animal is **hypersensitive**.

SUMM FAD can have manifestations of both immediate and delayed-type **hypersensitivity** (described in detail in Janeway et al., ibid.). Effective treatment of FAD has been difficult if not impossible to achieve.. . .

SUMM Thus, there remains a need to more clearly define flea saliva allergens capable of inducing a **hypersensitive** response in animals. In addition, there remains a need to develop a method to collect substantially pure flea saliva allergens. . .

SUMM . . . is about the same size as the reaction to the negative control solution. In particular, the method can detect immediate **hypersensitivity** and/or delayed **hypersensitivity**.

SUMM . . . or has allergic dermatitis. In particular, the method can be used to detect IgE antibodies as an indicator of immediate **hypersensitivity** in the animal.

DETD . . . from the bites of ectoparasites. A preferred ectoparasite saliva protein homologue includes at least one epitope capable of eliciting a **hypersensitive** response to the natural ectoparasite saliva protein counterpart. An ectoparasite saliva protein homologue can also include an epitope capable of. . . ability of an ectoparasite saliva protein homologue to detect and/or treat (i.e., immunomodulate or regulate by, for example, desensitizing) the **hypersensitivity** of an animal susceptible to or having allergic dermatitis, can be tested using techniques known to those skilled in

the. . .

DETD . . . sand flies, black flies, horse flies, horn flies, deer flies, tsetse flies, stable flies, myiasis-causing flies and biting gnats; ants; **spiders**, lice; mites; and true bugs, such as bed bugs and kissing bugs, including those carrying Chagas disease. Even more preferred. . .

DETD . . . invention can contribute to an epitope's ability to induce an allergic response against the protein in an immediate or delayed **hypersensitivity** response.

DETD . . . the present invention to carry out its function (e.g., anti-coagulation, anti-complement, vasodialators, proteases, acid phosphatases or detecting and/or treating the **hypersensitivity** of an animal susceptible to or having allergic dermatitis). A mimetope can be a peptide that has been modified to. . .

DETD One embodiment of the present invention is an in vivo test that is capable of detecting whether an animal is **hypersensitive** to ectoparasite saliva products. An in vivo test of the present invention can initially be used to determine if an animal is **hypersensitive** to ectoparasite saliva products and then used to determine if an animal is **hypersensitive** to a particular ectoparasite saliva component, in particular to an ectoparasite saliva protein. An in vivo **hypersensitivity** test of the present invention is particularly useful for identifying animals susceptible to or having allergic dermatitis. An in vivo **hypersensitivity** test of the present invention is even more useful for identifying animals susceptible to or having FAD. A suitable in vivo **hypersensitivity** test of the present invention can be, but is not limited to, a skin test comprising administering (e.g., intradermally injecting. . .

DETD . . . novel aspect, however, of the present invention is that an ectoparasite saliva product of the present invention can induce a **hypersensitive** response in the absence of an immunopotentiator.

DETD . . . positive control solution of the present invention contains an effective amount of at least one compound known to induce a **hypersensitive** response when administered to an animal. A preferred compound for use as positive control solution includes, but is not limited. . . histamine. A negative control solution of the present invention can comprise a solution that is known not to induce a **hypersensitive** response when administered to an animal. As such, a negative control solution can comprise a solution having compounds essentially incapable of inducing a **hypersensitive** response or simply a buffer used to prepare the formulation, such as saline. An example of a preferred negative control. . .

DETD **Hypersensitivity** of an animal to one or more formulations of the present invention can be evaluated by measuring reactions (e.g., wheal. . . syringes. Preferred devices for scratching include devices that permit the administration of a number of samples at one time. The **hypersensitivity** of an animal can be evaluated by determining if the reaction resulting from administration of a formulation of the present. . . the size of a wheal produced by administration of a positive control sample to an animal, then that animal is **hypersensitive** to the experimental sample. Conversely, if an experimental sample produces a reaction similar to the reaction produced by administration of a negative control sample to an animal, then that animal is not **hypersensitive** to the experimental sample.

DETD Preferred wheal sizes for evaluation of the **hypersensitivity** of an animal range from about 16 mm to about 8 mm, more preferably from about 15 mm to about. . .

DETD Preferably, the ability or inability of an animal to exhibit an immediate **hypersensitive** response to a formulation of the present invention is determined by measuring wheal sizes from about 2 minutes to about. . .

DETD Preferably, the ability or inability of an animal to exhibit a delayed **hypersensitive** response to a formulation of the present invention is determined by measuring induration and/or erythema from about 18 hours to. . . after administration of a sample, and even more preferably at about 24 hours after administration of a sample. A delayed **hypersensitivity** response can also be measured using other techniques such as by determining, using techniques known to those of skill in. . .

DETD Animals suitable and preferred to test for **hypersensitivity** to ectoparasite saliva proteins using a skin test of the present invention are disclosed herein. Particularly preferred animals to test. . .

DETD . . . allergic dermatitis by demonstrating that an animal has been previously exposed to an ectoparasite saliva antigen and, therefore may be **hypersensitive** to further exposure to an ectoparasite saliva antigen.

DETD According to the present invention, an in vitro **hypersensitivity** test of the present invention can be, but is not limited to, an immunoabsorbent test comprising: (a) contacting a formulation. . . dermatitis. The immunoabsorbent test is particularly useful for the detection of IgE antibodies in the body fluid, thereby indicating immediate **hypersensitivity** in the animal. Determining the amount of iminmunocomplex formed can include the step of separating depending on the mode of. . .

DETD . . . capable if being inserted into a test tube. Suitable and preferred flea saliva products for use with an in vitro **hypersensitivity** test of the present invention are as disclosed for a skin test of the present invention.

DETD A second step of a preferred in vitro **hypersensitivity** test of the present invention comprises contacting the coated substrate with a body fluid, such as serum, plasma or whole. . .

DETD A third step of a preferred in vitro **hypersensitivity** test of the present invention comprises contacting the immunocomplexes bound to the substrate with a compound capable of binding to. . .

DETD A fourth step of a preferred in vitro **hypersensitivity** test of the present invention comprises measuring the amount of detectable label bound to the solid substrate using techniques known. . .

DETD A **hypersensitive** animal is identified by comparing the level of immunocomplex formation using samples of body fluid with the level of immunocomplex. . . or equal to immunocomplex formation using a positive control sample, then the animal from which the fluid was taken is **hypersensitive** to the ectoparasite saliva product bound to the substrate. Conversely, if a body fluid sample results in immunocomplex formation similar to immunocomplex formation using a negative control sample, then the animal from which the fluid was taken is not **hypersensitive** to the ectoparasite saliva product bound to the substrate.

DETD A preferred embodiment of an in vitro **hypersensitivity** test of the present invention comprises the steps of: (a) contacting an ELISA plate, which is coated with a suitable. . .

DETD . . . for determining if an animal is susceptible to or has allergic dermatitis can include an in vivo or in vitro **hypersensitivity** test of the present invention as described in detail above. A kit of the present invention further comprises at least. . .

DETD . . . more different in vivo and/or in vitro tests can be used in combination for diagnostic purposes. For example, the immediate **hypersensitivity** of an animal to an ectoparasite saliva allergen can be tested using an in vitro immunoabsorbent test capable of detecting IgE antibodies specific for an ectoparasite saliva allergen in the animal's bodily fluid. While most animals that display delayed **hypersensitivity** to an ectoparasite saliva allergen also display immediate **hypersensitivity** to the allergen, a small number of animals that display delayed **hypersensitivity** to an allergen do not display immediate **hypersensitivity** to the allergen. In such cases, following negative results from the IgE-specific in vitro test, the delayed **hypersensitivity** of the animal to an ectoparasite saliva allergen can be tested using an in vivo test of the present invention.

DETD . . . formulation of the present invention. According to the present invention, the term treatment can refer to the regulation of a **hypersensitive** response by an animal to bites from ectoparasites. Regulation can include, for example, immunomodulation of cells involved in the animal's **hypersensitive** response or alteration of the ability of an ectoparasite to introduce allergens into an animal, for example by inhibiting the. . . particular, immunomodulation refers to modulation of antigen:antibody interactions resulting in inflammatory responses, immunosuppression, and immunotolerization of cells involved in a **hypersensitive** response. Immunosuppression refers to inhibiting an immune response by, for example, killing particular cells involved in the immune response. Immunotolerization. . .

DETD . . . response of the animal (i.e., immunomodulating the animal) so as to block (i.e., to inhibit, reduce or substantially prevent) a **hypersensitive** response by the animal upon subsequent exposure to allergenic components transmitted through bites from ectoparasites.

Such a therapeutic composition is useful for immunomodulating animals known to be **hypersensitive** to ectoparasite saliva products and animals susceptible to **hypersensitive** responses against ectoparasite saliva products.

DETD . . . membranes, cochleates or micelles. A soluble de-sensitizing compound of the present invention is useful for: (1) inhibiting a Type I **hypersensitivity** reaction by blocking IgE:antigen mediated de-granulation of mast cells; (2) inhibiting a Type III **hypersensitivity** reaction by blocking IgG:antigen complex formation leading to complement destruction of cells; and (3) inhibiting a Type IV **hypersensitivity** reaction by blocking **T helper** cell stimulation of cytokine secretion by macrophages. A membrane-bound de-sensitizing compound of the present invention is useful for: (1) inhibiting a Type II **hypersensitivity** reaction by blocking IgG:antigen complex formation on the surface of cells leading to complement destruction of cells; (2) inhibiting a Type II **hypersensitivity** reaction by blocking IgG regulated signal transduction in immune cells; and (3) inhibiting a Type IV **hypersensitivity** reaction by blocking T cytotoxic cell killing of antigen-bearing cells.

DETD . . . be covalently linked to a ligand molecule capable of targeting the de-sensitizing compound to a specific cell involved in a **hypersensitive** response to ectoparasite saliva products. Appropriate ligands with which to link a de-sensitizing compound include, for example, at least a. . .

DETD . . . accomplished by those skilled in the art. An effective dose refers to a dose capable of treating an animal against **hypersensitivity** to ectoparasite saliva allergens. Effective doses can vary depending upon, for example, the therapeutic composition used, the arthropod from which. . . doses to immunomodulate an animal against ectoparasite saliva allergens include doses administered over time that are capable of alleviating a **hypersensitive** response by an animal to ectoparasite saliva allergens. For example, a first tolerizing dose can comprise an amount of a therapeutic composition of the present invention that causes a minimal **hypersensitive** response when administered to a **hypersensitive** animal. A second tolerizing dose can comprise a greater amount of the same therapeutic composition than the first dose. Effective. . . comprise increasing concentrations of the therapeutic composition necessary to tolerize an animal such that the animal does not have a **hypersensitive** response to the bite of an ectoparasite. An effective dose to desensitize an animal can comprise a concentration of a therapeutic composition of the present invention sufficient to block an animal from having a **hypersensitive** response to the bite of an ectoparasite. Effective desensitizing doses can include repeated doses having concentrations of a therapeutic composition that cause a minimal **hypersensitive** response when administered to a **hypersensitive** animal.

DETD A suitable single dose is a dose that is capable of treating an animal against **hypersensitivity** to ectoparasite saliva allergens when administered one or more times over a suitable time period. For example, a preferred single. . . the original administration. Further treatments with the therapeutic composition preferably are administered when the animal is no longer protected from **hypersensitive** responses to ectoparasite. Particular administration doses and schedules can be developed by one of skill in the art based upon. . .

DETD A therapeutic composition of the present invention can be used in conjunction with other compounds capable of modifying an animal's **hypersensitivity** to ectoparasite bites. For example, an animal can be treated with compounds capable of modifying the function of a cell involved in a **hypersensitive** response, compounds that reduce allergic reactions, such as by systemic agents or anti-inflammatory agents (e.g., anti-histamines, anti-steroid reagents, anti-inflammatory reagents. . . chain class switching from IgE to IgG). Suitable compounds useful for modifying the function of a cell involved in a **hypersensitive** response include, but are not limited to, antihistamines, cromolyn sodium, theophylline, cyclosporin A, adrenalin, cortisone, compounds capable of regulating cellular. . .

DETD . . . products produced as described in Examples 2 and 3 include at least one allergenic protein capable of inducing an immediate **hypersensitive** response in a sensitized dog. In particular, injection of the mixtures of flea saliva antigens referred to as FS-1 and. . .

DETD . . . formulations produced as described in Examples 2 and 3 include at least one allergenic protein capable of inducing a delayed **hypersensitive** response in a sensitized dog. Injection of the mixtures of flea saliva proteins referred to as FS-1 and FS-2 induced. . .

DETD . . . in FIG. 5 through 9, indicate that saliva protein formulations of the present invention are sufficiently allergenic to induce a **hypersensitive** response in a sensitized dog. Numerous samples induced both an immediate **hypersensitive** response and a delayed **hypersensitive** response.

DETD This example demonstrates the ability of numerous flea saliva protein samples isolated in Examples 2 and 3 to induce a **hypersensitive** response by histopathology of tissue removed from selected lesions on the dogs described in Example 8.

DETD . . . mastocytic and eosinophilic, subacute dermatitis. Lesions noted in all the slide specimens examined are consistent with an allergic Type I **hypersensitivity** reaction.

DETD . . . 10 dogs with non-flea-related pruritic dermatoses including, but not limited to, atopy, food allergy dermatitis, pyoderma, seborrhea, and other parasitic **hypersensitivity** reactions; and (3) 10 dogs with normal skin and no history of chronic skin diseases. The dogs were of any. . .

DETD . . . 2.0 .mu.g E. coli-produced fspN3; (h) 0.2 .mu.g S. frugiperda-produced fspN3; and (i) 2.0 .mu.g S. frugiperda-produced fspN3. The immediate **hypersensitivity** results are shown in Table 20, and the delayed **hypersensitivity** results are shown in Table 21. Scoring was as described in Example 8; NA indicates a bad injection.

DETD . . . also exhibited a positive immediate reaction in 4 and all dogs, respectively. The two dogs that showed a strong delayed **hypersensitive** response reaction to FS-1 showed similar delayed **hypersensitive** response reactions to recombinantly produced fspH and fspN3.

=> d ti tot

L43 ANSWER 1 OF 9 USPATFULL
TI Ectoparasite saliva proteins and apparatus to collect such proteins

L43 ANSWER 2 OF 9 USPATFULL
TI Ectoparasite saliva proteins and apparatus to collect such proteins

L43 ANSWER 3 OF 9 USPATFULL
TI Ectoparasite saliva proteins and apparatus to collect such proteins

L43 ANSWER 4 OF 9 USPATFULL
TI Ectoparasite saliva proteins and apparatus to collect such proteins

L43 ANSWER 5 OF 9 USPATFULL
TI Ectoparasite saliva proteins and apparatus to collect such proteins

L43 ANSWER 6 OF 9 USPATFULL
TI Ectoparasite histamine releasing factor, genes and uses thereof

L43 ANSWER 7 OF 9 USPATFULL
TI Flea nucleic acid sequences and uses thereof

L43 ANSWER 8 OF 9 USPATFULL
TI Therapeutic compounds

L43 ANSWER 9 OF 9 USPATFULL
TI Therapeutic compounds

=> s l11 (s) (spider or jellyfish)
L44 3833 L11 (S) (SPIDER OR JELLYFISH)

=> s l40 (s) l44
L45 0 L40 (S) L44